

An Evaluation of the Effectiveness of Community-based Direct Observation of Treatment (CDOT) for Tuberculosis Compared to Health-Centre Direct Observation of Treatment (HC-DOT) in Cambodia



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Abstract

Introduction

Cambodia suffers very high rates of tuberculosis (TB). In 1994, Hospital Direct Observed Treatment (DOT), as recommended by WHO, was introduced. In 2002 ambulatory or health center DOT (HC-DOT) was implemented, requiring patients to come to the HC to take medicine with HC staff during the intensive phase. In 2005, community-based DOT (CDOT), using health volunteers in their own community, was implemented in some areas. This study compares CDOT and HC-DOT in terms of treatment success, case notification and acceptability.

Methods

This thesis includes a systematic review and meta-analysis of studies comparing CDOT to HC-DOT and Family-DOT; a controlled before-after quantitative study of the introduction of CDOT (1067 participants in 48 HCs with all TB forms were surveyed at the baseline in 2002/2003, as were 1297 in 2006/2007 two years after its introduction); and a qualitative study assessing its strengths, weaknesses and acceptability to HC staff, patients and CDOT watchers.

Results

The meta-analysis from the systematic review shows that CDOT was at least as effective as HC-DOT (RR=1.05, CI: 1.01-1.10), and treatment of smear-positive patients treated by CDOT is clearly better than for family-DOT (OR=1.33, CI: 1.20-1.48)

The quantitative study shows that in Cambodia the treatment success rates of patients treated with CDOT and HC-DOT are similar (OR=1.26, 95% CI: 0.56-2.82). In the CDOT areas, the death rate among all TB patients was significantly reduced after its implementation (OR=0.37, 95%CI: 0.15-0.92)

Most participants in the qualitative study felt CDOT was helpful particularly for very sick patients, and because it reduced travel costs and allowed patients to continue working. There was significant involvement of family members in both approaches.

Conclusion

CDOT is as effective as HC-DOT for treatment success and case finding. Both approaches are well accepted. There remain problems which need to be addressed in order to improve outcomes.

Doctorate in Public Health Integrating Statement

The research degree Doctorate in Public Health (Dr.PH) at London School of Hygiene and Tropical Medicines (LSHTM) aims to provide candidates with access to a wide range of skills and experience in various disciplines related to public health management and research. There are three components which are required for Dr.PH candidates.

1. Taught courses on leadership and management, systematic reviews, research methodologies, how to transfer policies into practice and various study units selected by individual candidate. All are examined.
2. A Professional Attachment (PA) in an institution related to the candidate's particular interest. The purpose of the PA is to provide the candidate with understanding of leadership and management, the organizational structures in public health organizations, and in particular to show that the candidate has developed an extensive understanding as a public health person as well as a policy maker. The PA is accomplished with a marked report.
3. The final component is a research project that leads to a dissertation. This is designed to contribute to knowledge of the topic through the individual candidate's thought and analysis.

This dissertation continues from my Master thesis on "how to improve TB case detection rates in Cambodia" at Boston University, United States. My main interest is in TB and in particular how to extend TB treatment to patients who live in remote areas. The taught courses, including on systematic reviews, research methodology and design, and getting results into policy and practice, allowed me to understand the fundamentals of research.

The course in public health leadership and management provided me with the abilities and instruments for my personal management development.

Between September 2005 and March 2006 I carried out a Professional Attachment (PA) to the Cambodian National Public Health Promotion Department in Phnom Penh, Cambodia. The aim of the PA was to identify the organizational structure, and to examine how staff are organized and how decisions are made in the context of public health. For the PA I used qualitative methods including both formal and informal interviews with staff at all levels, and observation of interactions during meetings between staff within all units. By analyzing the transcripts of interviews and notes from the observation, I gained new skills in methods of qualitative data and analysis. The PA enabled me to expand my knowledge and perspective of organizational management, leadership and the process of decision making, in a public health organisation.

During my PA, I discussed many issues relating to health activities and programmes with staff at the Ministry of Health. Between 2005 and 2006 the NTP started to implement CDOT with the main purpose of increasing TB case detection rates and maintaining treatment success rates, and in particular improving patients' adherence to treatment. I was interested to know how effective of the new CDOT was compared with the existing ambulatory DOT in Cambodia. In developing the methodology for my research, it was interesting for me to conduct the systematic review to see how the effectiveness of CDOT compared to alternative DOT options in different settings. I also carried out the qualitative study in this research, because I wanted to explore what patients, staff, and DOT watchers think of CDOT and ambulatory DOT, in particular how both DOT approaches work in the field.

Working for the Dr.PH degree has been very important to me; it has brought me new skills such as leadership and management in the public health field, and expanded my understanding of public health within the academic scientific structure. In particular it is enabling me to take a role in policy and decision making.

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Statement of Own Work

LONDON SCHOOL OF HYGIENE & TROPICAL MEDICINE

I have read and understood the School's definition of plagiarism and cheating given in the Research Degrees Handbook. I declare that this thesis is my own work, and that I have acknowledged all results and quotations from the published or unpublished work of other people.

Signed:.....by C PICH

Date:

Full name: CHANMONY PICH (please print clearly)

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LIST OF ABBREVIATIONS

CDOT	Community Directly Observed Treatment
CENAT	National Centre for Tuberculosis and Leprosy Control
CHC	Cambodian Health Committee
CHW	Community Health Worker
CPA	Complementary Package of Activities
CRS	Catholic Relief Services
DOTS	The international recommended strategy for TB control
DOT	Directly Observed Treatment
Extra-P	Extra Pulmonary Tuberculosis
GFATM	Global Fund to Fight AIDS, Tuberculosis and Malaria
HC	Health Centre
HC-DOT	Health Centre Directly Observed Treatment
HIV	Human Immunodeficiency Virus
JICA	Japan International Cooperation Agency
LSHTM	London School of Hygiene and Tropical Medicine
MDR	Multi-Drug Resistance
MoH	The Ministry of Health
MPA	Minimum Package of Activities
NGO	Non Governmental Organization
NTP	National Tuberculosis Control Program
OD	Operational District
PEV	Promotion of Education and Vaccination

PHC	Primary Health Care
PHD	Provincial Health Department
PFHAD	Partners for Health and Development
RACHA	Reproductive And Child Health Alliance
RCTs	Randomised Control Trials
RH	Referral Hospital
SCA	Save the Children Australia
SM(+)	Smear pulmonary positive
SM(-)	Smear pulmonary negative
TB	Tuberculosis
USAID	United States Agency for International Development
VHSG	Village Health Support Group
WHO	World Health Organization
WRC	Women's Relief Corp

Definition of terms

- **Hospitalized DOT (this is neither CDOT nor HC-DOT):** treatment in which patients swallow TB drugs in the hospital under the direct observation of health workers (HWs) during the intensive phase of treatment.
- **Ambulatory DOT (HC-DOT):** treatment in which non-hospitalized patients swallow TB drugs at the health facility under direct observation of HWs. Patients attend the health facility every morning during the intensive phase of treatment.
- **DOT at home:** this is a type of community based DOT in which treatment takes place at the patient's house under the direct observation of HWs or an instructed person during the intensive phase of treatment. DOT at home is sub-divided into "DOT at home by health worker" and "DOT at home by community member" called Community DOTS.
- **Community DOT (CDOT):** forms part of DOT at home, whereby TB patients stay in their community during treatment and receive DOT from a person selected from the community, who is not a health worker. These individuals are called DOT watchers or DOT observers.
- **Multi-drug resistant patient:** a patient resistant to at least two TB drugs which are Rifampicine and Isoniazide

Source: Guidelines on Community DOTS Implementation. NTP, Cambodia

1 CHAPTER 1: Background and Rational

This chapter introduces the international recommended strategy for TB control known as DOTS, and discusses the effectiveness of directly observed treatment (DOT), and the contribution of the community in TB care. It also describes the background for the research in the context of the epidemiology of TB, the impact of TB, the health care system and the national TB control programme in Cambodia.

1.1 Global tuberculosis burden

Tuberculosis (TB) is one of the leading causes of adult mortality (Dye C and al 1999). It is estimated that 32% of the world's population has been infected with TB (Borgdorff MW, Nagelkerke NJ et al. 1999), and between 8.5-9.2 million TB cases were estimated in 2010 (WHO 2011). It is estimated that globally around 1.1 million deaths caused by TB, it was equivalent to 15 deaths per 100 000 population in 2010 (WHO 2011).

More than 90% of these global TB cases and deaths occur in the developing world, where 75% of cases are found among the most economically productive age group (15-54 years). Each year, about 80% of all new cases occur in Africa and Southeast Asia (Dye C and al 1999). Because HIV significantly increases the risk of developing TB (Narain JP, Raviglione MC et al. 1992), the number of TB cases will be larger in countries with a high prevalence of both diseases (Msamanga GI and Fawzi WW 1997). According to WHO, in 2010 there were around 0.35 million deaths among people who were HIV-positive (WHO 2011).

In addition, multi-drug resistance TB (MDR-TB), which is exacerbated or caused partly by poorly managed TB treatment, is a growing problem in many countries (Dye C and al 1999) . In 2010, 650 000 cases of MDR-TB were reported among the world's 12.0 million prevalent TB cases (WHO 2011)

1.2 DOTS TB control strategy

Recognizing an urgent need to deal with these problems, in 1993 the World Health Organization (WHO) declared TB to be a global emergency and developed a cost-effective health intervention to fight the disease (WHO 1994; WHO 2002), the DOTS TB control strategy (Enarson D A, Rieder H L et al. 2000). This strategy has been reported to be successful in both developed and developing countries including the United States (Bayer R, Stayton C et al. 1998), Bangladesh (Chowdhury A M R 1997), China (Programme 1996), and South Africa (Wikinson D 1994). In addition, DOTS has been shown to be highly cost-effective (Baltussen R 2005).

DOTS combines five elements that must be fully implemented to achieve effective TB control: 1) A government commitment to sustained TB control activities; 2) Case detection through bacteriological examinations of patients with respiratory symptoms attending primary health care units; 3) A standardized treatment regime of six to eight months for at least all sputum smear positive cases, with directly observed therapy (DOT) for at least the initial two months; 4) Securing a regular, uninterrupted supply of all essential anti-TB drugs; and 5) A standardized recording and reporting system, allowing monitoring and evaluation of treatment results (WHO 2006). The DOTS strategy focuses on two operational targets which are promoted by WHO: detection of at least 70% of the new smear-positive TB cases and cure of at least 85% of these cases (WHO 1994;

Enarson D A, Rieder H L et al. 2000; WHO 2002). According to WHO estimates, with direct observation of treatment it is anticipated that the number of contacts infected would be reduced by 40%, and 80% of deaths attributed to TB worldwide would be prevented (Myer CS 1996). By the end of 2004, 83% of the world's population lived in the countries covered by DOTS (WHO 2006), and today more than 30 million patients with TB have been treated with DOTS, resulting in cure rates of more than 80%. However, case detection has remained low at 42% in 2003 (Dye C 2003), but has increased steadily over the years. By the end of 2006, the case detection rate for new-smear positive cases reached 61% (WHO 2008), and it is estimated that it will reach the target of 70% in 2012 if all national TB control programmes (NTPs) are fully implementing DOTS (Dye C 2002; Dye C 2003).

However, a key problem in TB control still remains, which is how to encourage patients' adherence to treatment. Adherence requires many components such as appropriate health care, including diagnosis and information about their disease, accessible health care, including drugs supply and help to complete the treatment (CDC 1993).

1.3 The effectiveness of Directly Observed Therapy (DOT)

Directly Observed Therapy (DOT) as already stated above aims to decrease the risk of TB infection by increasing treatment adherence and thus cutting the chain of transmission, reducing morbidity and mortality, and preventing the development of drug resistance (Dye C 1998; Enarson D A, Rieder H L et al. 2000). Initially, DOT was implemented in the setting of the hospital or clinic. The advantage of clinical settings is that patients can be closely monitored by staff which may encourage adherence (Sumartojo 1993). However, the effectiveness of implementation in hospitals and clinics has been

questioned, especially for those badly affected by HIV-related TB in sub-Saharan Africa (WHO 2003). According to the qualitative review by Munro S et al 2007 (Munro S, Lewin. S et al. 2007), for patients on DOT who live near to hospitals or clinics, the time needed to be present for direct observation for a full course of treatment is not necessarily a significant barrier, as clinics are easily accessible to them. However, in areas where patients live far from the hospital or clinic, lack of transportation, cost of travel, the inconvenience of the treatment time, the challenge of disabilities and travel, and time lost from attending daily tasks, were stated as posing barriers. Moreover, other qualitative studies have reported that discrimination against TB patients can be a problem, and some patients resist going to collect their drug supplies at clinics because of discriminatory staff behavior (Steen TW 1999); also women have reported issues of safety while travelling, as well as the stigma of visiting a clinic for treatment (Khan M 2005) .

The Cochrane systematic review of randomised controlled trials (RCTs) of the effectiveness of DOT for TB treatment by Garner and Volmink showed no significant difference between type of DOT and self-supervision at home (Volmink J and Garner 2003; Garner P and Volmink 2007). Garner and Volmink also noted in this review that DOT is also often difficult to implement and requires a great deal of effort from both patients and health care providers through regular attendance at the health center (Volmink J and Garner 2003). However; in 2007, Noyes and Popay conducted a systematic review of qualitative research focusing on lay experiences and perceptions of TB treatment (Noyes J and Popay J 2007). They concluded that the effectiveness of TB control program cannot be judged by DOT itself. They confirmed reports that barriers to accessing and complying with treatment depend on the factors discussed below in section 1.4, and that DOT could have the most negative impacts on the poorest patients who had

the most to lose from loss of earnings because of the need to attend for treatment and to pay of transport, who had the most to fear from disclosure of the disease, and who were most at risk of TB stigmatization. They concluded that DOT was least effective when the primary focus was on direct observation itself rather than on the supportive nature of treatment (Noyes J and Popay J 2007).

The key challenge of DOT is to implement it well, maximizing the convenience to and respectful interaction with patients, recognizing that DOT is necessary both to fulfill society's obligations to care for individual patients effectively, and to protect the rest of society by preventing the development and spread of TB, including drug-resistant strains.

1.4 Tuberculosis and adherence to the treatment

Drugs for TB have been available since the 1940s, yet three million people a year continue to die from it, with those in low income countries at high risk of death (Netto EM 1999). TB treatment is long and intensive, lasting at least six to eight months, and the side effects are often severe including vomiting, loss of appetite and insomnia. This can lead to poor adherence, with WHO reporting in 2012 that globally about 0.4 million cases of diagnosed TB have treatment changed to a retreatment regime, because their previous treatment has failed or defaulted (WHO 2012).

The qualitative systematic review by Munro et al in 2007 (Munro S, Lewin. S et al. 2007) reported poor adherence caused not only by the side effects of drugs, but by other factors such as problems at health facilities including long waiting times, lack of privacy for patients, and the absence of staff during patients' visits. Poor relationships between patients and staff, inadequate follow-up by staff, and maltreatment by providers resulting

in non-adherence, has also been reported from different settings (Munro S, Lewin. S et al. 2007). The distance and availability of transport as well as the physical condition of the patient, are key issues for patients' adherence; patients cannot attend regularly if their homes are far from the health center (Munro S, Lewin. S et al. 2007). Poverty and disadvantageous circumstances influence the decision to seek and continue treatment. Poor patients are less able to give up work or risk the loss their jobs in order to come for treatment at health facilities (Noyes J and Popay J 2007). Moreover, the issue of TB stigmatization is a key factor resulting in non-adherence; patients say they are reluctant to find or come back for treatment, as they wish to keep the diagnosis and treatment secret (Munro S, Lewin. S et al. 2007; Noyes J and Popay J 2007). The review by Noyes and Popay (Noyes J and Popay J 2007) has stated that poor adherence is also caused by lack of financial and social support from family members or friends, and women are more likely than men to experience negative family attitudes and are less likely to receive financial support. With low adherence, not only does TB remain uncured, but it can cause prolonged infectiousness, relapse of TB, multi-drug resistance (MDR-TB) and death. Poor adherence not only increases the health risk for the individual, but also for the community. In 2010, 290 000 cases of MDR-TB were estimated to exist among patients with pulmonary TB world-wide (WHO 2011).

1.5 Community-based direct observation treatment (CDOT)

Because of poor adherence; WHO has recommended expanding DOT from health facilities into communities, by engaging members of the community such as health workers, health volunteers and neighbors as DOT supporters in providing community-based DOT, with the aims of reducing mortality rates due to TB by decreasing the

distance between providers and patients, and thus removing some of the barriers to treatment compliance (Maher D 1999; WHO 2003).

The involvement of the community in TB care can promote access to effective TB services by bringing the delivery of health services as close as possible to those who need them, and by extending access to TB care to the poor, who need it most, so help reduce the TB mortality rate (Maher D 1999; WHO 2003). Community involvement in TB care is clearly a contribution to, and not a substitute for other national tuberculosis programme activities. Communities have contributed to TB services by supervision of treatment under DOT; patient support groups for the support and motivation of patients; and community education, so as to increase community awareness of the disease and its treatment.

Many non-randomised controlled trials have been conducted especially in developing countries including in sub-Saharan Africa, to investigate the community involvement in DOT programs. These studies have shown that involvement of the community in DOT can encourage patients to complete the treatment and can increase the accountability of local health services to the community (Hadley M and Maher 2000; Maher 2003; Maher D 2003). Based on these studies WHO encouraged the national TB programs, health care providers and communities to work together to increase community involvement in TB care, particularly DOT. The Global Plan to Stop TB expected that all developing countries, especially countries in Africa, would have scaled up community-based DOT, known as CDOT (WHO 2006 PART III).

The method of implementation of CDOT varies from study to study and between countries. Some countries have implemented CDOT to maintain high cure rates and to increase case identification, while others have implemented CDOT to improve adherence to treatment and to reduce the work load in the health facilities. The CDOT programs also vary in other characteristics such as the choice of a community supervisor. Some programs use health workers and health volunteers as DOT supporters, while others utilize patients' neighbors or family members. There are questions concerning the choice of community supervisors; some programs consider that family members can be DOT supervisors, whereas others regard family observation as a seductive but risky concept (Frieden TR and Sbarbaro 2007).

This aim of the current study, conducted in Cambodia, was to compare the outcomes of health center-DOT and community-based DOT in terms of case finding and treatment success, to determine the strengths and weaknesses of each, and to assess the relative acceptability of health center and community-based DOT to patients, health center staff and DOT watchers. The background for this study is described in the next section.

1.6 Country setting

1.6.1 Cambodia

Cambodia is an agricultural country of 181,035 square kilometers situated on the South-western Indo-Chinese Peninsula in Southeast Asia. It is bounded by Thailand, Vietnam, and Lao People's Democratic Republic. Cambodia comprises 24 provinces and municipalities, 183 districts, 1600 communes, and 13 406 villages. (Figure 1)

Figure 1: Map of Cambodia



According to the 2010 census, the total population is about 15 million, with 80% of the population living in rural areas and the remaining 20% in urban areas. It is estimated that the proportion of children less than 15 years is 42.8% and 51.8% of the population is female. The majority of the population is ethnic Khmer by ethnicity and Buddhist by religion (NISS 2010).

1.6.2 The health care system in Cambodia

Since 1994, the Ministry of Health has been committed to reorganizing the health system, placing an emphasis on the district level (MoH 1997). The system reforms, which focus on delivering essential health services to rural areas where the majority of the population live, have led to the establishment of “Operational health Districts (ODs)” comprising a referral hospital (RH) and a network of around 10 health centers (HCs). HCs provide the

basic health needs of the majority of the population and serve a catchment area of approximately 10 000 people living in 2-3 communes of about 5-10 villages each (MoH 2007).

Each HC provides a basic integrated package of health care services referred to as the Minimum Package of Activities (MPAs). These services comprise basic preventive, promotive and curative care, including prenatal care, immunization, birth spacing, prevention of micronutrient malnutrition, and treatment of diarrhea and acute respiratory infection as well as TB. The referral hospital (RH), for its part, receives cases referred from the HCs and manages complicated cases, operations, serious illnesses requiring admission, and inpatients. These services are called the Complementary Package of Activities (CPAs) (MoH 2007).

Based on the 2010 Cambodia MoH report, in 2009, there were 8 national hospitals, 77 operational districts, 79 referral hospitals, 984 HCs and 111 health posts within the 24 provinces (MoH 2010).

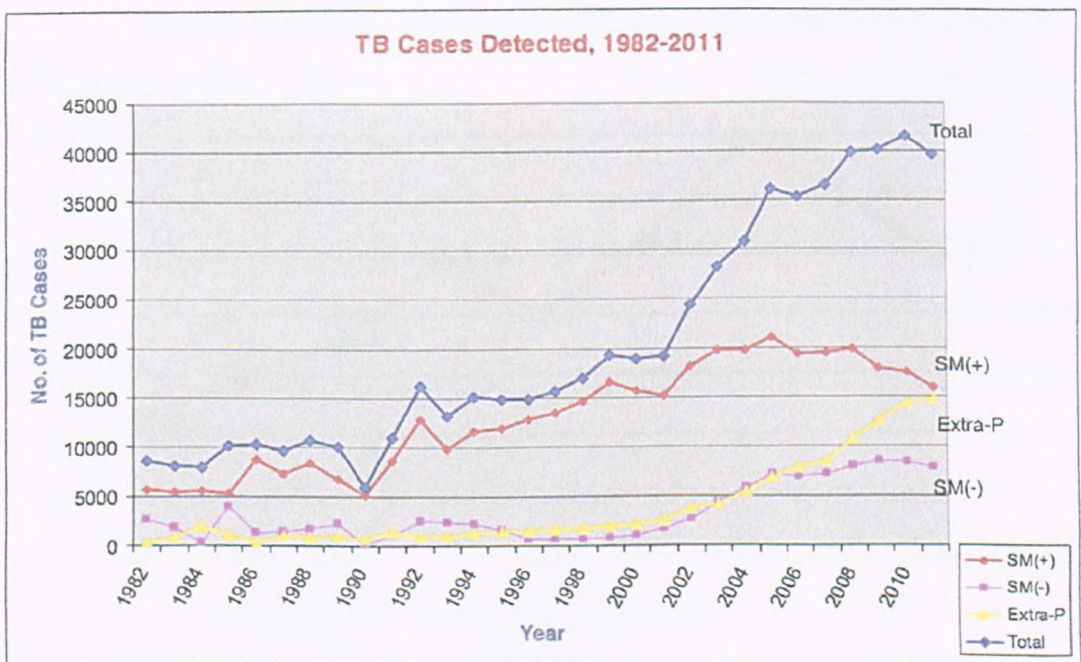
1.7 TB epidemiological context in Cambodia

Cambodia ranks 21st on the list of 22 countries which have the highest burden of tuberculosis (TB) in the world (WHO 2002); it is estimated that approximately 64% of the total population has been infected with TB (WHO 2000) and a substantial number of cases remain undetected. As of 2010, there were 41,628 new TB cases notified in Cambodia (WHO 2011); the estimated incidence rate of all forms of TB was 437 cases per 100,000 population and the prevalence rate of TB was 660/100,000 population (WHO 2011). The mortality rate from TB was 61/100 000 population in 2010 (WHO 2011).

TB continues to be among the major public health problems in the country mainly due to the HIV/AIDS epidemic in Cambodia. The number of notified TB cases increased from 8,000 in 1982 to about 41,628 in 2010 (MoH 2010). Since the Ministry of Health was re-established in 1980, TB notification rates slowly increased until about 1991, after which it started gradually to rise, especially the notification rates of smear positive TB. The current number of TB cases notified is estimated to be at the peak. It should also be noted that the increase is partly due to better diagnosis and case reporting. Figure 2 shows the TB case notification rates in Cambodia over approximately the past thirty years.

Figure 2: TB case notification (per 100 000 population) from 1982 to 2010

TB Cases Notification, 1982-2011

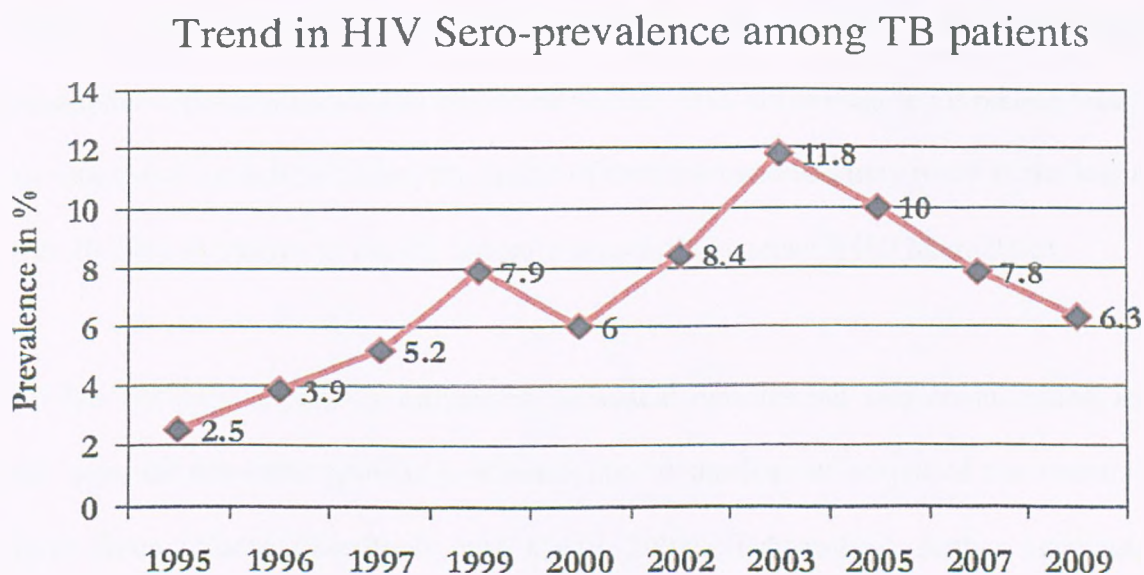


Source: National Tuberculosis Control Program in Cambodia (MoH 2010)

1.7.1 HIV-TB Co-infection in Cambodia

As noted, Cambodia is among the countries with a high incidence of combined TB and HIV/AIDS. The prevalence of HIV among people with TB increased drastically from 2.5% in 1995 to 10% in 2005 (MoH 2005), but has since fallen to 7.8% in 2007 and 6.3% in 2009 (MoH 2010). In 2010, 32,236 TB patients with known HIV status were reported (WHO 2011). Figure 3 shows the trend of prevalence of people with HIV among TB patients.

Figure 3: The Prevalence of people with HIV/AIDS among TB patients from 1995-2009



Source: National Tuberculosis Control Program in Cambodia (MoH 2010)

1.7.2 Multi-drug Resistance TB (MDR-TB)

MDR-TB is not a significant problem in Cambodia. According to the NTP survey in 2009, only 1.6% of the new TB cases were MDR-TB. The survey showed that by the end of 2010, 136 patients were registered and treated for MDR (MoH 2010).

1.8 The economic impact of TB in Cambodia

According to NTP around 62,000 people were estimated to suffer from TB and almost 9,000 Cambodians with TB died in 2010 (MoH 2010). The impact of TB on individuals includes not only physical health, but also economic, social and mental health. The economic impact may include negative effects on households and the country. Tuberculosis is considered a chronic disease because it requires at least six months treatment. Thus, the disease can drive people into deep poverty especially among households with incomes already below the poverty line. On average a TB patient loses 3 to 4 months of work time during the period of treatment and this may result in the loss of up to 20-30% of income in the TB patient's household income (WHO May, 2002).

This has not only negatively influenced individual families but also communities, and even national economic growth is affected due to the loss of output of the country's labour force (Nhem CheaBunly and Myers 2002). Tuberculosis further aggravates poverty because it drains national resources to fight it. Furthermore, due to lack of funds, Cambodia has to borrow money from outside sources such as from the World Bank. Thus TB contributes to creating national debt (Nhem CheaBunly and Myers 2002).

1.9 The National Tuberculosis (and Leprosy) Programme in Cambodia

1.9.1 DOTS Strategy

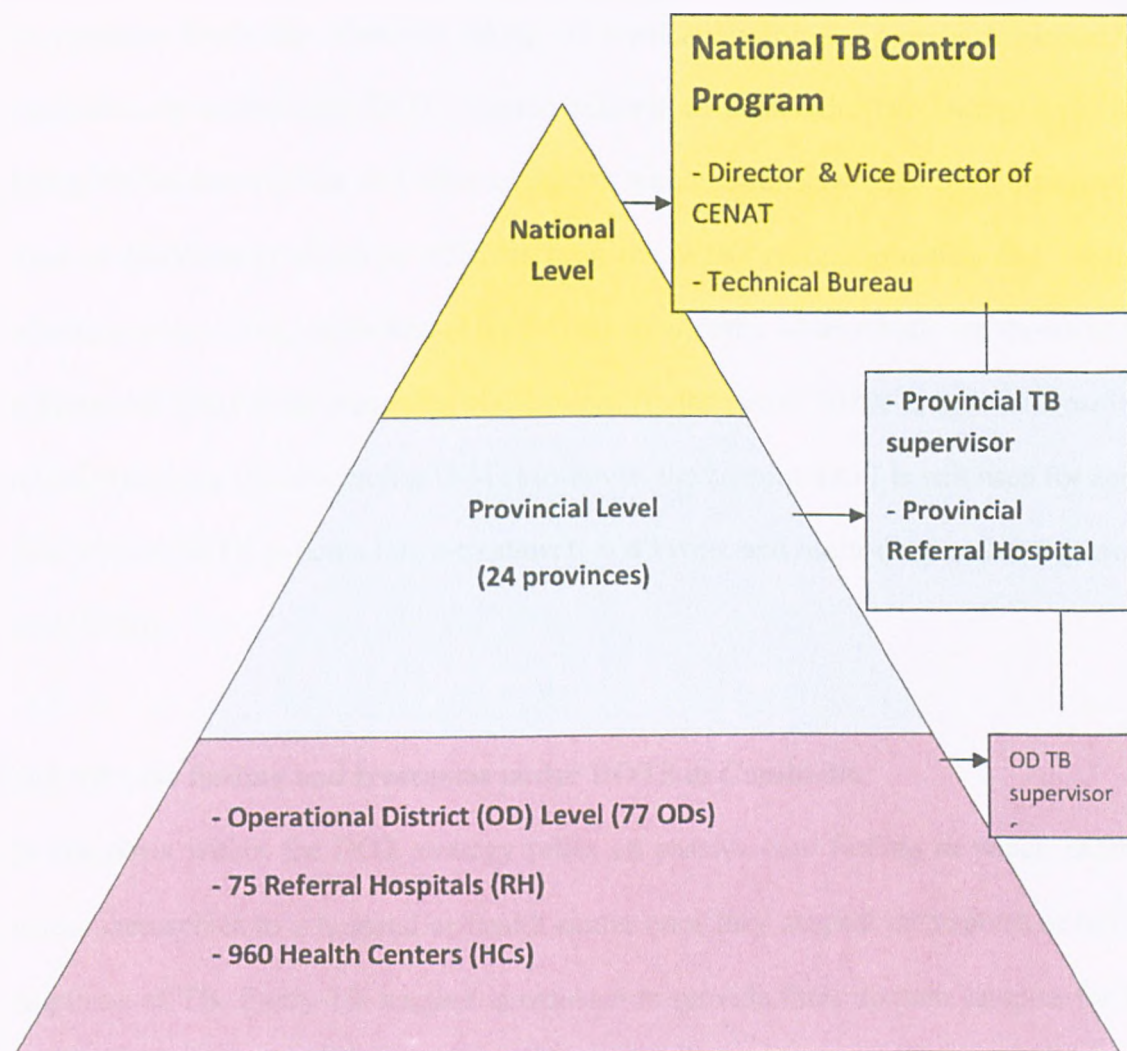
Nearly three decades of chronic internal conflict seriously damaged the health system in the country. The number of people with TB increased due to the poor health care system and living conditions were often unhygienic during this period. Recognizing an urgent need to deal with the catastrophic effects of TB, Cambodia's government – through the Ministry of Health, the National Tuberculosis Control Program (NTP) was initiated in 1980 with its main goal being to improve the health of the Cambodian people through the reduction in morbidity and mortality rates due to TB. Despite the fact that the NTP was fully committed to the TB intervention programme such as increasing TB awareness and providing health education to the general population for reducing the death due to TB, the NTP was not fully effective; for example in 1980s the cure rate for smear positive cases was only 69% and the case detection rate just 44% (MoH 2001).

In 1994, the DOTS strategy was introduced and adopted by the Ministry of Health. The treatment approach used at that time was mainly “hospitalization” DOT. Since 1995, the NTP has attained and maintained the objective of obtaining more than an 85% cure rate of infectious cases. For example, the cure rates for smear positive cases were 85% in 1995, 89% in 2001, 90% in 2005, 93% in 2007 and 95% in 2010 (MoH 2010). However, the case detection rate has remained relatively low (65% in 2010) compared to the 70% WHO target, and the prevalence (660/100 000 population) and incidence of TB in Cambodia is still among the highest in the world (WHO 2011).

Over the last decade, the burden of TB has increased in Cambodia due to human immunodeficiency virus infection. This could lead to an increased burden on the health services because of the associated morbidity and mortality. This may lead to health service exhaustion and forces patients to attend health centers often. In Cambodia, improving health service coverage and increasing the number of health workers to decrease workloads in health centers and reduce patients' cost seems a distant possibility.

In 2002, the NTP was decentralized into existing HCs supported by a vertical component of expertise in management, capacity building, monitoring and evaluation at national and provincial level. At the national level there are now three structures: the NTP headquarters, the TB referral hospital offering clinical and para-clinical TB services, and the National TB reference laboratory. At the provincial level, TB units and HC are responsible for program planning and management including training and supervision (MoH October, 2006). The structure of TB control in Cambodia is shown in Figure 4.

Figure 4: Structure of TB control in Cambodia



Source: National Tuberculosis Control Program (NTP), Cambodia (MoH 2010)

1.9.2 DOT implemented in Cambodia

Directly observed therapy for TB is one component of the DOT strategy, which requires someone to observe patients taking medicines everyday during the treatment. In Cambodia, today, there are three main DOT approaches: 1) Hospitalization DOT which requires patients to stay in a hospital for taking medication in the intensive phase, 2)

Ambulatory DOT which requires patients to come to a health facility to swallow drugs during the intensive phase, 3) and DOT at home, including community DOT, which uses the patient's home for observed taking of medication for six months treatment. In Cambodia, the ambulatory DOT requires patients to attend the HC taking medicines during the intensive phase and allows patients taking medicines with DOT watchers at home or community, which is different from the WHO recommendation that requires patients to come taking medicines at the HC for six months. More details are shown in the definition of terms at the beginning of the thesis. By the end of 2010, 75 referral Hospitals and 960 HCs were implementing DOT. Moreover, the hospital DOT is still used for about 10%-20% of all TB patients for re-treatment, and severe and multi-drug resistant patients (MoH 2010).

1.9.3 TB case finding and treatment under DOTS in Cambodia

TB diagnosis within the DOT strategy relies on passive case finding in which patients present themselves to a hospital or health center once they suspect themselves of having symptoms of TB. Every TB suspect is required to provide three sputum samples for TB diagnosis. Patients are taken to be tubercular if any of two sputum specimens are positive for Acid Fast Bacilli (AFB). Chest X-ray is rarely performed and is only available at a few hospitals in the cities due to its high cost. Diagnosis of smear negative and extra-pulmonary TB patients follows a clinical algorithm (MoH October, 2006).

TB treatment is mainly through hospitalized DOT and ambulatory DOT within the country. The duration for treatment is six months with Rifampicin, Isoniazid, Pyrazinamid, as well as Ethambutol during the first two month intensive phase (MoH 2010).

Under the ambulatory DOT, TB patients have to come to the health facility daily in the morning for two months for direct observation of treatment, supervised by the health facility staff. Follow-up of patients is done by checking sputa for AFBs after two months of treatment, after five months and at the end of the treatment period (MoH 2001; MoH 2010; MoH October, 2006).

1.10 Statement of the problem

It is more than eighteen years since the NTP implemented the DOT strategy in Cambodia. Experience from this programme implementation for nearly two decades showed the following findings. In the first five years, the DOT strategy was delivered mainly through hospital DOT. The case detection rate and cure rate increased compared with the previous implementation. However, this implementation did not completely reach its target due to many patients failing to adhere to treatment.

In 2002, the DOT program expanded from hospitals to HCs which implemented ambulatory DOT. This required patients to attend a HC everyday for the intensive phase to take TB medication under the observation of HC staff. This approach was more acceptable to patients because they could return to their families and continue to work. However, it did not completely address the issue of acceptability or affordability for people living far from a HC. It also increased the social costs to the patient, and the economic burden on the family, and may discourage adherence to treatment (Munro S, Lewin. S et al. 2007).

Although the application of the DOT strategy enables Cambodia to achieve and maintain the treatment success rate of 95% and reduce mortality rate in the country, many issues

still exist. It is possible that whereas DOT coverage is 100% in the urban areas, the problem of accessibility still exists in remote areas, especially for those which are far from the city or from health facilities. Information on DOT services in the country is still sparse and due to weak health management or minimal information, many TB patients are unaware of the services and NTP may be detecting only patients living near the health facilities (Suchi M and Tateno 2002).

As recommended by the WHO, community-based DOT has been introduced into Cambodia by the NTP in collaboration with Non Governmental Organizations (NGOs) and piloted in some rural areas in Cambodia since 2004. Community-based DOT (CDOT) was established to improve case finding through referral of TB suspects by communities, to improve adherence to treatment, to improve TB case management, and to reduce the financial burden for patients and their families. CDOT requires community support by volunteer workers who are properly trained and who are regularly supervised by staff from the referral health facility and/or staff from the NTP. They also have the task of providing medicines and other supplies such as sputum containers, recording and reporting material and information on TB knowledge (MoH 2004).

Various community DOT models have been implemented in different settings by using different types of DOT supervisors to complement health center-based DOT (HC-DOT) (David W and Geraint 1997; Colvin M 2003; Singh A.A 2004; Wandwalo E 2004; Clarke M 2005). However, the key question that remains is who is an appropriate and suitable community DOT supervisor and how can the motivation and sustainability of these projects in a resource constrained setting be maintained, without compromising the quality of TB control. Some places have used community health workers and chiefs of the

village as the DOT supervisors (Becx-Bleumink M 2001; Kironde S and Kahirimbanyi 2002; Dudley L 2003; Cavalcante S.C 2007) while others have used friends, neighbours, family members (Boogaard van den J 2009; Zimbisayi Zvavamwe and Ehlers 2009) and former TB patients (Demissie M 2003). There is variation in TB treatment supervision from place to place and the challenge remains to determine what sort of supervision is best in different settings because it could affect patients' adherence to treatment.

Since CDOT was established in Cambodia, there have been only two evaluations (Khieu K 2007; Frances Daily and Men July, 2004). In 2004, a cross - sectional study of CDOT was undertaken in three provinces in Cambodia (Frances Daily and Men July, 2004). The study reported that all CDOT pilot areas showed an increase in TB case detection rates and that patients were extremely satisfied with the ability to receive treatment within their communities. In addition, it reported that in some areas, DOT watchers were involved in providing drugs and in observing patients taking their medication only in the first two months of treatment (Frances Daily and Men July, 2004). This study did not assess treatment outcomes in the areas where CDOT was piloted. Furthermore, the study did not show by how much the case detection rate was increased compared to the rate before the pilot study. Another 2007 study used a cohort design with retrospective data, and was conducted in two ODs in order to compare the results of TB treatment between HC-DOT and CDOT (Khieu K 2007). The study suggested that CDOT was as effective as HC-DOT: no significant difference in cure rates was found between HC-DOT (90.2%) and CDOT (92.5%) for people with smear positive TB. However no description was given of how the CDOT was implemented, there was no description of who the DOT watchers were, and the methodology of the study has several potential limitations including the study design, as the data was collected retrospectively without a control group, and the

sample size was small (n= 1269 patients). The authors did not report where the data came from, and did not include the new TB case finding after CDOT was implemented.

The implementation of CDOT varies between countries, and its operation in Cambodia in terms of structure and sponsors has never been studied, particularly in rural areas where the infrastructures are weak and resources limited. Thus, there has not been a systematic scientific study of how successful the implementation of CDOT is in terms of case notification and treatment outcome within the areas of applied CDOT and the concepts and experiences of people and community using CDOT.

For this reason, the purpose of this research is to examine how CDOT differs from the health facilities approach in terms of their working structures and the results they produce, including treatment success and case notification. The research uses two approaches. The first is a quantitative study that was designed as a controlled before-after introduction of CDOT to compare the outcomes of health center DOT (HC-DOT) and CDOT in terms of case finding and treatment success. The second approach is a qualitative study to explore how HC-DOT and CDOT are functioning, to determine their strengths and weaknesses, and to assess the acceptability of community and health centre based DOT to health centre staff, TB patients and DOT watchers.

1.11 Research Team

The author of this study (a Dr.P.H Candidate) was responsible for the research project, including the methodology design, the implementation of the research, directing research assistants for data collection, conducting in-depth interviews for qualitative study, double-checking data entry, and analysis, the documentation and interpretation of the

findings, the discussion, conclusions and recommendations, as well as the reporting and dissemination of the findings.

Ten research assistants were employed to help with the quantitative data collection of the main study. One statistician, who works at the National Institute of Statistics in the Ministry of Planning, helped with the data cleaning and data entry for the quantitative study. In addition, one doctor who works at the National Institute of Public Health (NIPH) helped with data re-entry and guided the author for the quantitative analysis. One note taker from the NIPH was employed for the in-depth interviews.

The main supervisors from the London School of Hygiene and Tropical Medicine (LSHTM), Professor Joy Townsend, Professor Mark Petticrew and Dr. Simon Lewin (Norwegian Knowledge Centre for the Health Services, Oslo) provided the author with guidance and support throughout the project.



Picture 1: Author with the research team from the NTP and Dr. Mao Tan Eng (Director of the NTP) in front of a health centre



Picture 2: Author with research assistance team: Planning Session

1.12 Organisation of the thesis

The thesis is divided into ten chapters. Chapter 1 describes the state of global TB, DOTS TB control strategy as recommended by WHO, and the effectiveness and limitations of DOT, and CDOT. The setting for the study, the epidemiology of TB, National TB control programme and implementation of DOT are also described in Chapter 1. Chapter 2 presents a systematic review of the effectiveness of CDOT compared to alternative DOT delivery options for people requiring treatment for clinically active TB, or prevention of active disease. The pilot study for the quantitative and qualitative aspects of the project including the quality of data are described in Chapter 3. The methods of the quantitative study are described in Chapter 4. Chapter 5 presents the results of treatment outcomes between CDOT and health centre-based DOT from the quantitative study. Chapter 6 describes the methods of the qualitative study. The qualitative results relating to the implementation of DOT treatment and its administration are presented in Chapter 7. Chapter 8 presents the qualitative results relating to the implementation of the CDOT program. The qualitative data on the HC-DOT program are presented in Chapter 9. Finally, Chapter 10 presents the discussions, recommendations and conclusions of the research.

1.13 Timeline of the study

The proposal of this study was reviewed and approved by the committee at LSHTM in May, 2008, and the pilot study took place in August 2008. The data collection was conducted in January, 2009 for nine months. However, the analysis and present of data collection in this study was delayed due to personal and health problems. The author had to take an interruption of studies for 2 years during this period; firstly because of two sessions of maternity leave and secondly for a period of health treatment. The data

analysis of this study was therefore completed in 2012, almost three years after the data was collected.

2 CHAPTER 2: Systematic review and meta-analysis of studies of effectiveness of CDOT compared to alternative DOT delivery options

This chapter reports the systematic review of the evidence on the effectiveness of community-based DOT as delivered through different DOT providers in different settings. The objective of the systematic review is to review the effectiveness of CDOT compared to alternative DOT delivery options for people requiring treatment for clinically active tuberculosis, or prevention of active disease.

2.1 Methods for systematic review

A systematic review of randomised and non-randomised trials examining the effectiveness of CDOT was conducted following PRISMA guidelines (Liberati A, Altman DG et al. 2009).

2.1.1 Inclusion criteria

A Type of studies

Randomised control trials (RCTs) and non-randomised control trials (non-RCTs) were included in the review. The non-RCTs included case-control studies, prospective, retrospective cohort studies and before and after studies that compare two programs, CDOT and alternative DOT options.

B Type of participants

People requiring treatment for clinically active TB or on medication for preventing active TB were included in the review. However, the review excluded studies of patients with multi-drug resistance TB or HIV.

C Type of intervention

As mentioned above, the type of DOT supporters for CDOT programmes varies from one country or setting to another, and in some settings CDOT was defined as using community health workers or health volunteers, but not family members as DOT watchers (Fred L 2003; Eliud W 2004; Singh A.A 2004). In this review, CDOT, the intervention group, is defined as routine direct observation by community health workers or health volunteers, known as DOT watchers, observing patients taking their anti-tuberculosis drug in their community, in their home, in the home of the community health workers or in a location other than a health facility.

D Type of control group

There were two types of control group. The first DOT control group was the health facility- based DOT (HC-DOT) defined as patients observed receiving their treatment at health facilities. The second control group was family-based DOT defined as patients receiving their treatment at home with family members responsible for observing patients taking their medicines. We included the family-DOT as a control group because family DOT is another feasible DOT strategy recommended by WHO. Family DOT was used in some settings where health volunteers were not available in the community (Pungrassami P 2002; Okanurak K., Kitayaporn D. et al. 2007)

E Type of outcome measures

The primary outcome in the review is treatment success among smear positive TB patients, which is the sum of cure and treatment completion. WHO standard outcome definitions for cure, completion, failure and default were used^a. Studies which did not provide stratified outcome data for CDOT programs alone were excluded. Moreover, self-supervised therapy was excluded from the review because this program is not considered as a DOT program (Enarson D A, Rieder H L et al. 2000).

2.1.2 Search methods for the review

A search was carried out to identify randomised and non-randomised studies (with no language restriction) using databases PubMed, CINAHL, EMBASE, and the Cochrane Central Register of controlled trials Central (<http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/fs.html>). The detail of combinations of search terms and concepts shows in Appendix 1.

^a “Cured patients” were defined as those with sputum smear positive before starting treatment and confirmed to be sputum negative at five (or six) months on at least one occasion. Patients who completed the full course of treatment but have had no sputum taken at the end of treatment are defined as “Treatment Completion”. Patients, who remain or become smear positive at five (or six) month or later during treatment, are classified as “Treatment Failures”. “Default” is defined as patients who fail to collect drugs for more than two consecutive months during treatment.

Source: http://www.stoptb.org/wg/gli/assets/documents/TBcasedefinitions_20110506b.pdf

Searches were conducted from 1995 until 2012 because DOT has been fully implemented only since 1994. The key word tuberculosis and TB were combined with keywords about, using keywords “tuberculosis, directly observed therapy DOT, community based DOT, community involvement, health centre DOT, health facility based DOT, and patients’ adherence”. Hand search of the International Journal of Tuberculosis and Lung Disease was carried out from 1995 to 2012. Also searched were published bibliographies of related topics, and citations in articles which were included in this review.

2.1.3 Selection of RCTs studies

RCTs were selected in this review, studies in which either individual patients or places where patients lived were randomly allocated to either the intervention (CDOT) or control groups (health facility DOT or family DOT), in order to compare the treatment success between these two groups. Because of the nature of the intervention, most RCTs studies were unblinded.

2.1.4 Selection of non-RCTs studies

Non-RCTs in this review were defined as studies that included intervention and control groups in order to assess the treatment success of the intervention compared with the control, but where participants were not randomised. Before and after studies are included in this group because they assess the treatment success for participants in the intervention areas before and after the CDOT started compared to control areas which only implemented health facility DOT or family DOT.

2.2 Description of studies

In the initial search, 314 studies were identified. Based on the inclusion criteria, this number was narrowed down to 22 studies (see Table 1 of studies included in the review).

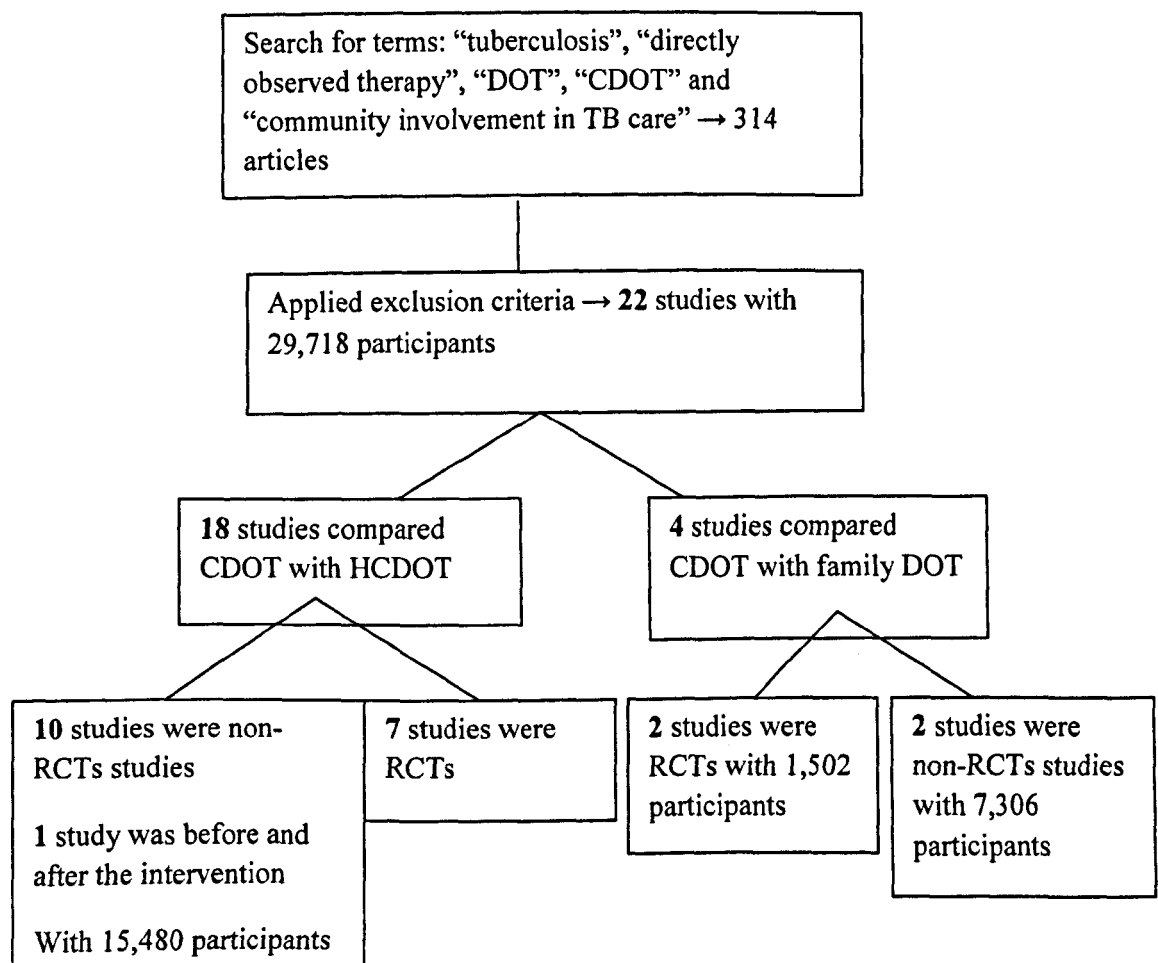
Twenty two studies in total satisfied the inclusion criteria. Seven studies (Zwarenstein M 2000; Fred L 2003; Eliud W 2004; Singh A.A 2004; Clarke M 2005; Nirupa C 2005; Daniel G. Datiko 2009) were RCTs, comparing the treatment outcomes between CDOT and health facility-based DOT. Eleven studies (Becx-Bleumink M 2001; Kironde S and Kahirimbanyi 2002; Arora V.K 2003; Demissie M 2003; Dudley L 2003; Cavalcante S.C 2007; Khieu K 2007; Boogaard van den J 2009; Zimbisayi Zvavamwe and Ehlers 2009; Kabongo D and B 2010; André P. Gabriel and Mercado 2011) were non-RCTs. All were conducted in low-income or middle-income countries, and evaluated the effectiveness of CDOT compare to health facility-based DOT in TB care.

A further four studies, two RCTs (Wright J 2004; Newell JN 2006) and two non-RCTs (Mathew A 2005; Anuwatnonthakate A 2008), compared the treatment success between CDOT and family-DOT. The period of observation for these was confined to the first two months of treatment (intensive phase) in some and in others it was for the full treatment period.

Eleven of the studies (Zwarenstein M 2000; Becx-Bleumink M 2001; Demissie M 2003; Fred L 2003; Singh A.A 2004; Clarke M 2005; Nirupa C 2005; Newell JN 2006; Daniel G. Datiko 2009; Zimbisayi Zvavamwe and Ehlers 2009; André P. Gabriel and Mercado 2011) included only smear positive pulmonary TB patients, while the others included patients with all TB forms (smear positive, smear negative and extra-pulmonary TB).

29,718 participants in total were included in the review. Appendix 2 shows all studies included in the review. Appendix 3 shows studies excluded from the review. Figure 5 shows the flow of studies through the review.

Figure 5: Flowchart showing flow of studies through the review



2.3 Data analysis

This review used meta-analysis methods to synthesise the data. The analysis is organized into two parts. The first part assessed the treatment success for smear-positive TB of CDOT compared with the health facility-based DOT. In this part, the analysis was done

separately for the RCTs and non-RCTs. Outcomes from the seven RCTs were analyzed using the risk ratio (RR) while the other ten non-RCTs were analyzed using odds ratios (OR), with 95% confidence intervals (CI) to assess estimated effects. A random-effects model was used when there was statistically significant heterogeneity (chi square $P < 0.1$); and the fixed-effect model when the heterogeneity was not statistically significant (chi square $P > 0.1$) (Senn S 2007).

The second comparison examined treatment success for smear-positive TB of CDOT compared with family-DOT. Due to only four studies being included in this review, the analysis combined the RCTs and non-RCTs studies by using the OR, with 95% confidence intervals (CI) in order to estimate the overall effects.

2.4 Description of outcomes

This review assessed the effectiveness of implementing CDOT, by comparing the TB treatment success for smear-positive TB of CDOT with other DOT alternatives such as health facility DOT or family DOT. According to the WHO standard, treatment success includes both cure and treatment completion. Other outcomes such as death, failure, defaulter and transfer out, are classified as unfavourable outcomes (WHO 2008) in the review.

2.5 Characteristics of community-based DOT (CDOT)

Patients treated by CDOT in these studies were supervised by treatment supervisors who were former TB lay health workers, health education assistants, community volunteers, or community health workers (CHWs) (Zwarenstein M 2000; Dudley L 2003; Fred L 2003; Singh A.A 2004; Clarke M 2005; Nirupa C 2005; Cavalcante S.C 2007; Khieu K 2007;

Boogaard van den J 2009; Daniel G. Datiko 2009; Zimbisayi Zvavamwe and Ehlers 2009; Kabongo D and B 2010; André P. Gabriel and Mercado 2011). Treatment supervisors were trained to observe drug-taking, to encourage patients to complete treatment, and to keep records and collect drugs (Zwarenstein M 2000; Arora V.K 2003; Demissie M 2003; Fred L 2003; Singh A.A 2004; Clarke M 2005; Nirupa C 2005; Khieu K 2007; Boogaard van den J 2009; Daniel G. Datiko 2009; Kabongo D and B 2010). Patients were observed daily taking the medications by treatment supervisors at the patient's home (Arora V.K 2003; Demissie M 2003; Singh A.A 2004; Cavalcante S.C 2007; Boogaard van den J 2009) or the treatment supervisor's home (Zwarenstein M 2000; Fred L 2003; Wright J 2004; Mathew A 2005; Nirupa C 2005; Newell JN 2006; Khieu K 2007; Daniel G. Datiko 2009; Zimbisayi Zvavamwe and Ehlers 2009) for at least two months of the intensive phase. Treatment supervisors were responsible for encouraging patients to complete treatment by following-up patients who failed to adhere to treatment. In addition, treatment supervisors were responsible for referring others in the community with TB-like symptoms, to a health facility ((Daniel G. Datiko 2009).

2.6 Characteristics of alternative DOT delivery options

Two DOT delivery options are compared with community-based DOT in the review. The first option is health facility-based DOT where patients were observed at least five days per week taking the medications by staff at a health facility (Zwarenstein M 2000; Becx-Bleumink M 2001; Kironde S and Kahirimbanyi 2002; Arora V.K 2003; Demissie M 2003; Dudley L 2003; Fred L 2003; Singh A.A 2004; Clarke M 2005; Nirupa C 2005; Cavalcante S.C 2007; Khieu K 2007; Boogaard van den J 2009; Daniel G. Datiko 2009; Zimbisayi Zvavamwe and Ehlers 2009; Kabongo D and B 2010; André P. Gabriel and Mercado 2011). The second comparison is with the family-based DOT; patients were

supervised by a family member, spouse or partner at home. Family members or carers were trained to observe drugs- taking, to keep records, and to collect drugs from the health facilities (Wright J 2004; Mathew A 2005; Newell JN 2006; Anuwatnonthakate A 2008).

2.7 Assessment of study quality

2.7.1 RCTs study

All RCT studies included in the review were of necessity unblinded with the intervention group supervised by community members, while the control consisted of patients assisted by staff at health facilities (Zwarenstein M 2000; Fred L 2003; Eliud W 2004; Singh A.A 2004; Clarke M 2005; Nirupa C 2005; Daniel G. Datiko 2009) or by family members (Wright J 2004; Newell JN 2006). Four studies were cluster randomised controlled trials ((Fred L 2003; Eliud W 2004; Clarke M 2005; Daniel G. Datiko 2009).

Patients' allocation to treatment group in four studies was randomised by coin tossing(Eliud W 2004), assigned by medical officers (Singh A.A 2004; Nirupa C 2005) and computer-generated random sequences(Zwarenstein M 2000). All of the trials were unblinded (Zwarenstein M 2000; Fred L 2003; Eliud W 2004; Singh A.A 2004; Clarke M 2005; Nirupa C 2005; Daniel G. Datiko 2009). More than 10% of participants were excluded from the analysis in the study by Fred (Fred L 2003). Three trials did not report sufficient information on methods of follow up (Singh A.A 2004; Nirupa C 2005; Daniel G. Datiko 2009). In the remaining RCTs fewer than 10% of participants were lost to follow up (Zwarenstein M 2000; Eliud W 2004; Clarke M 2005). Reasons for dropout included discontinuation of CDOT in some health facilities in the intervention group

(Clarke M 2005), change of treatment methods from CDOT or HC-DOT to self-supervision (Zwarenstein M 2000) or interruption of treatment (Eliud W 2004).

Four studies (Zwarenstein M 2000; Fred L 2003; Eliud W 2004; Clarke M 2005) were analysed by intention to treat (Newell 1992). The baseline characteristics in three trials (Zwarenstein M 2000; Eliud W 2004; Clarke M 2005) were similar in that loss to follow-up was less than 10%, and the selection bias and confounding factors were controlled for in their analysis.

Two trials comparing treatment outcomes between CDOT and family DOT (Wright J 2004; Newell JN 2006), assigned participants to CDOT or family DOT based on random selection of papers from a basket; the outcome assessment was blinded, and fewer than 10% of participants were lost to follow up.

2.7.2 Non-RCTs

Seven of the eleven non-RCTs comparing CDOT and HC-DOT programs, were prospective cohort studies (Kironde S and Kahirimbanyi 2002; Arora V.K 2003; Demissie M 2003; Dudley L 2003; Zimbisayi Zvavamwe and Ehlers 2009; Kabongo D and B 2010; André P. Gabriel and Mercado 2011), three were retrospective cohort studies (Cavalcante S.C 2007; Khieu K 2007; Boogaard van den J 2009), and one study was a before and after study (Becx-Bleumink M 2001). Participants were assigned to intervention group or control group based on patients' choice – i.e whether they wanted to be treated with the DOT watcher in the community or staff at the health facility (Kironde S and Kahirimbanyi 2002; Arora V.K 2003; Demissie M 2003; Dudley L 2003;

Cavalcante S.C 2007; Zimbisayi Zvavamwe and Ehlers 2009; André P. Gabriel and Mercado 2011).

One study (Becx-Bleumink M 2001) compared the treatment outcomes and TB case-finding before and after the introduction of CDOT in 1998. The baseline data was collected in 1996-1997. The allocation of participants into CDOT or health facility-based DOT was based on patients' choice.

Two studies compared the treatment outcomes between CDOT and family DOT (Mathew A 2005; Anuwatnonthakate A 2008). The allocation of patients to CDOT or family DOT was based on patients' choice (Mathew A 2005). The outcome assessment was unblinded in all the eleven cohort studies.

2.8 Results

2.8.1 Community-based DOT versus health facility-based DOT

A Randomised controlled trials (RCTs)

Comparing the seven trials (Zwarenstein M 2000; Fred L 2003; Eliud W 2004; Singh A.A 2004; Clarke M 2005; Nirupa C 2005; Daniel G. Datiko 2009), there is a very small but statistically significant difference in the treatment success for smear-positive TB between the CDOT and HC-DOT (RR=1.05, CI: 1.01-1.10) in the RCTs. There is no significant heterogeneity among the seven studies (chi-square=8.27, df=6, p=0.219). See Figure 6.

Pooling only the five RCTs (Fred L 2003; Eliud W 2004; Singh A.A 2004; Nirupa C 2005; Daniel G. Datiko 2009) with a large sample size, there is no statistically significant

difference in the treatment success for smear-positive TB between the CDOT and HC-DOT (RR=1.035 CI: 0.99-1.08). See Figure 7. It suggests that treatment outcomes for smear-positive patients in the CDOT were not better than HC-DOT, but were at least as successful as HC-DOT.

Figure 6: CDOT versus HC-DOT in RCTs

Comparison: Community based DOT versus Health centre based DOT

Outcome: Treatment success (cure + treatment completion) for smear-positive TB

Type of study: Randomised control trials

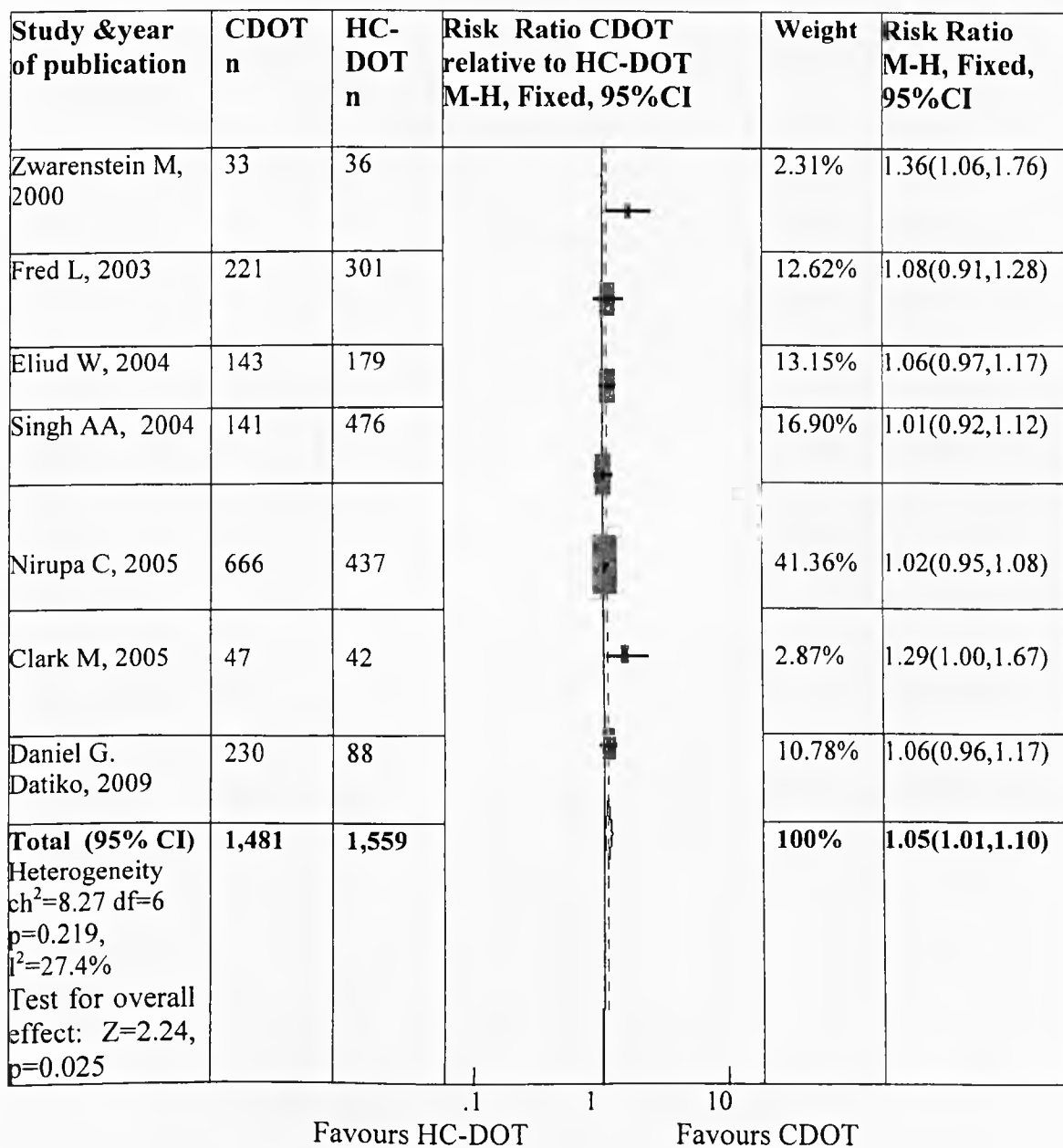
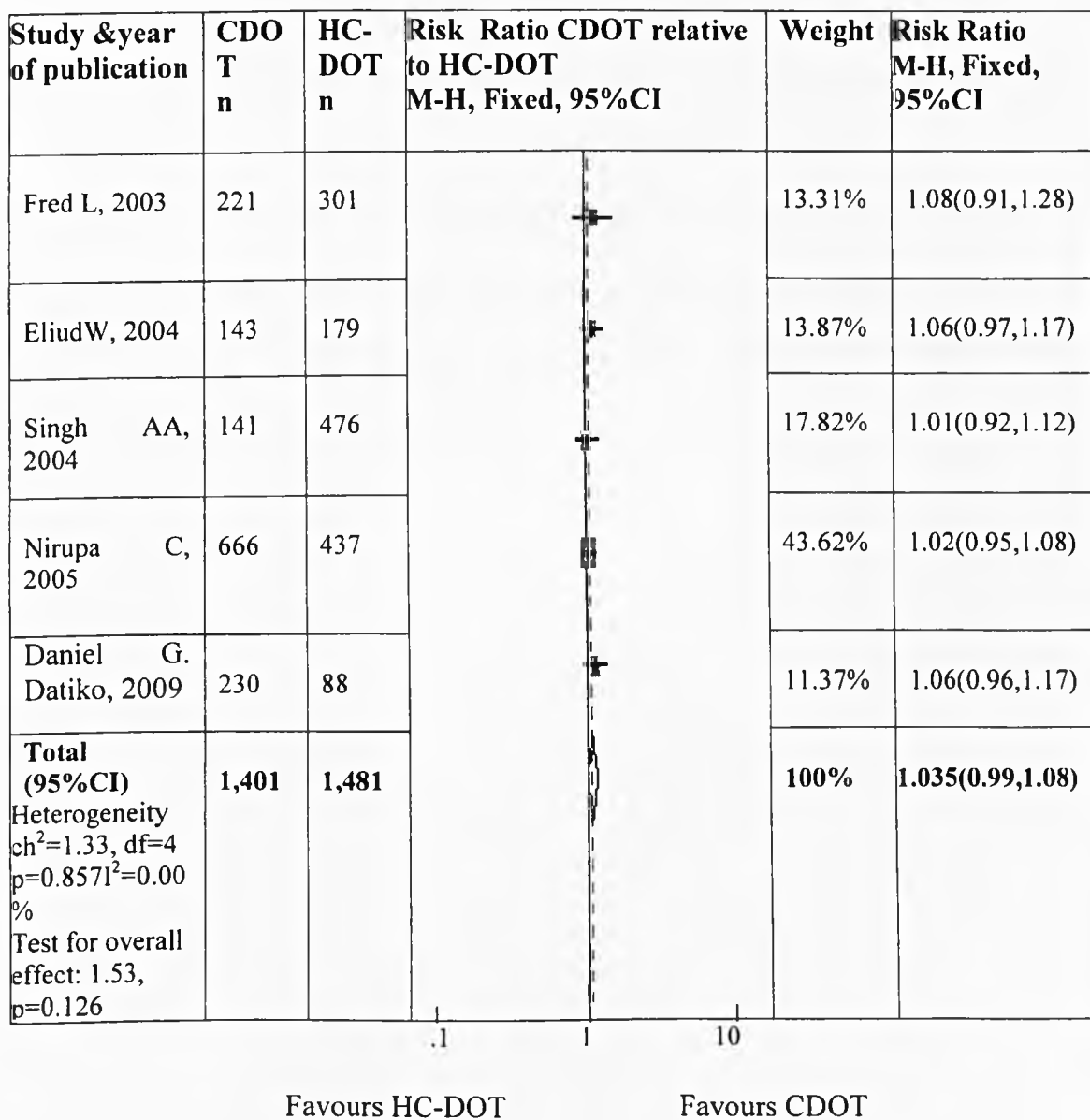


Figure 7: CDOT versus HC-DOT in the five larger RCTs

Comparison: Community based DOT versus Health centre based DOT

Outcome: Treatment success (cure + treatment completion) for smear-positive TB

Type of study: Randomised control trials with a large sample-size



B Non-RCTs

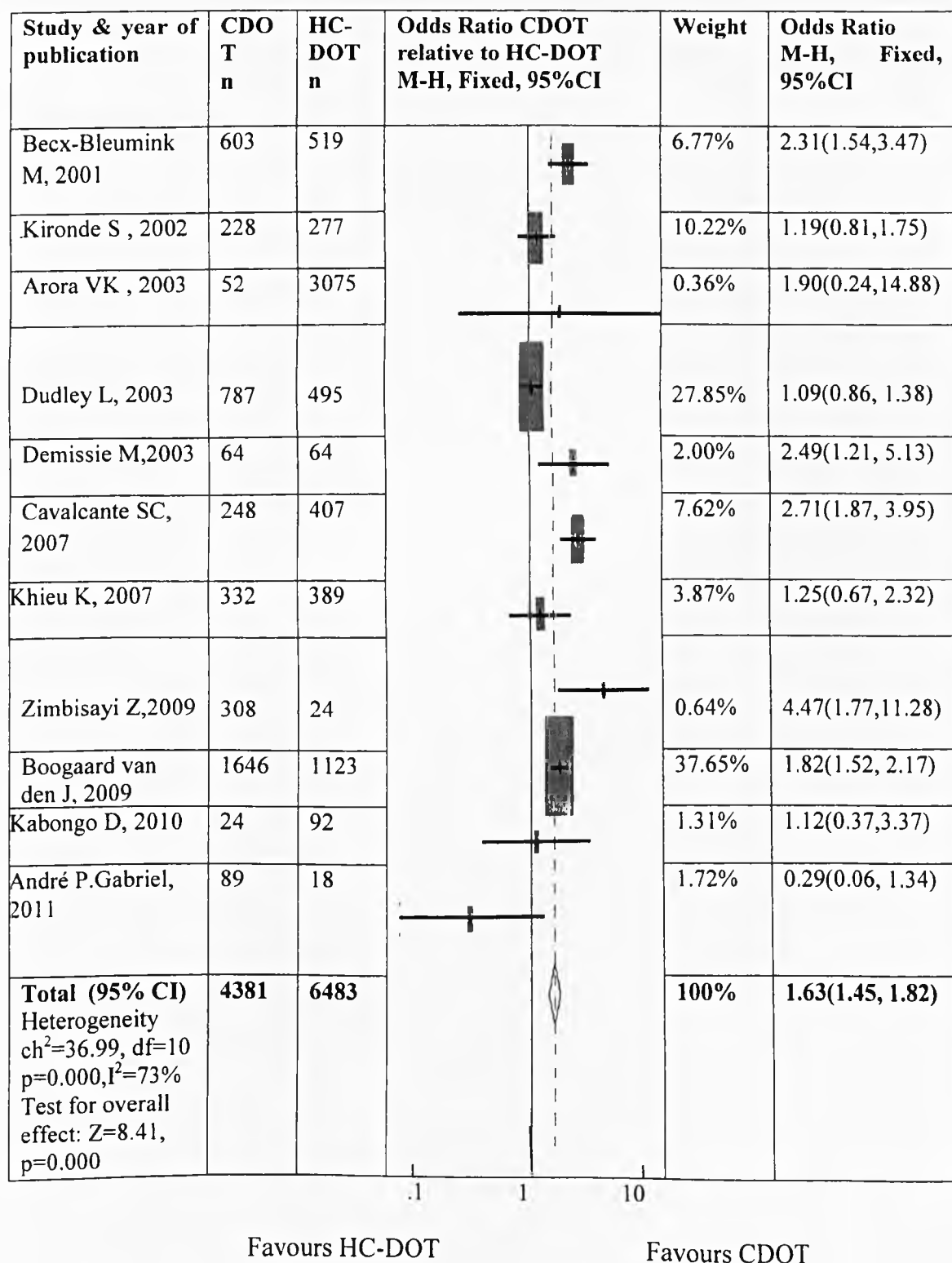
The meta-analysis of non-RCTs found substantial heterogeneity across the eleven studies (Becx-Bleumink M 2001; Kironde S and Kahirimbanyi 2002; Arora V.K 2003; Demissie M 2003; Dudley L 2003; Cavalcante S.C 2007; Khieu K 2007; Boogaard van den J 2009; Zimbisayi Zvavamwe and Ehlers 2009; Kabongo D and B 2010; André P. Gabriel and Mercado 2011) ($\chi^2=36.99$, $df=10$, $p<0.0001$). In contrast with the results of the RCTs, the treatment success for smear positive TB for patients treated under CDOT is significantly and substantially better than that for HC-DOT (OR=1.63, CI: 1.45-1.82). See Figure 8. It indicates that treatment outcomes for smear-positive patients treated by the CDOT was better than for those treated by HC-DOT. This may be biased by patient choice of treatment.

Figure 8: CDOT versus HC- DOT in non-RCTs

Comparison: Community based DOT versus Health centre based DOT

Outcome: Treatment success (cure + treatment completion) for smear-positive TB

Type of study: non-randomised control trials



2.8.2 CDOT versus family-based DOT

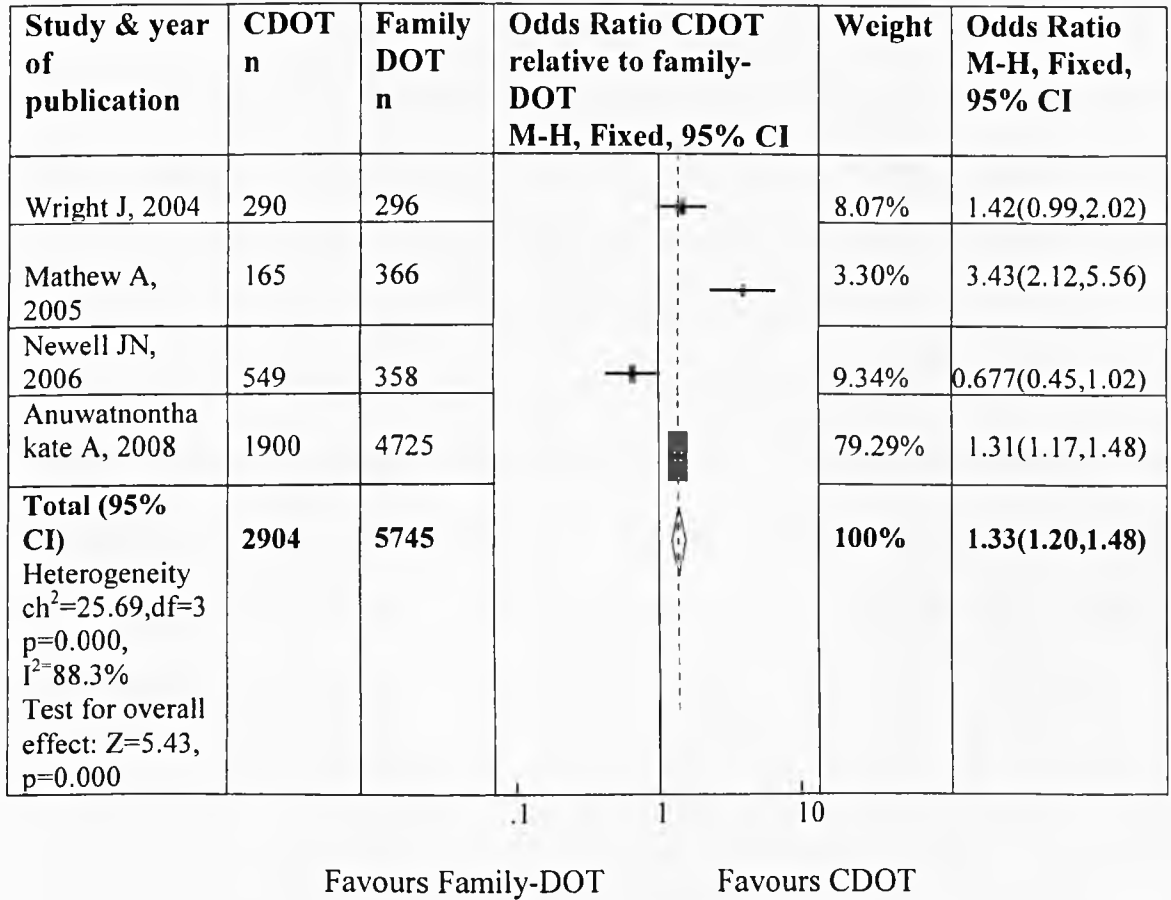
The odds of success for smear-positive patients treated by CDOT was greater than for family-based DOT programs (OR=1.33, CI: 1.20-1.48); but with significant heterogeneity among the four studies (chi-square=25.69, df=3, $p<0.0001$). The results are shown in Figure 9. They are strongly influenced by the large study by Anuwatnonthakate (Anuwatnonthakate A 2008)

Figure 9: CDOT versus family-based DOT

Comparison: Community based DOT versus Family-based DOT

Outcome: Treatment success (cure + treatment completion) for smear-positive TB

Type of study: Randomised control trials and non-RCTs

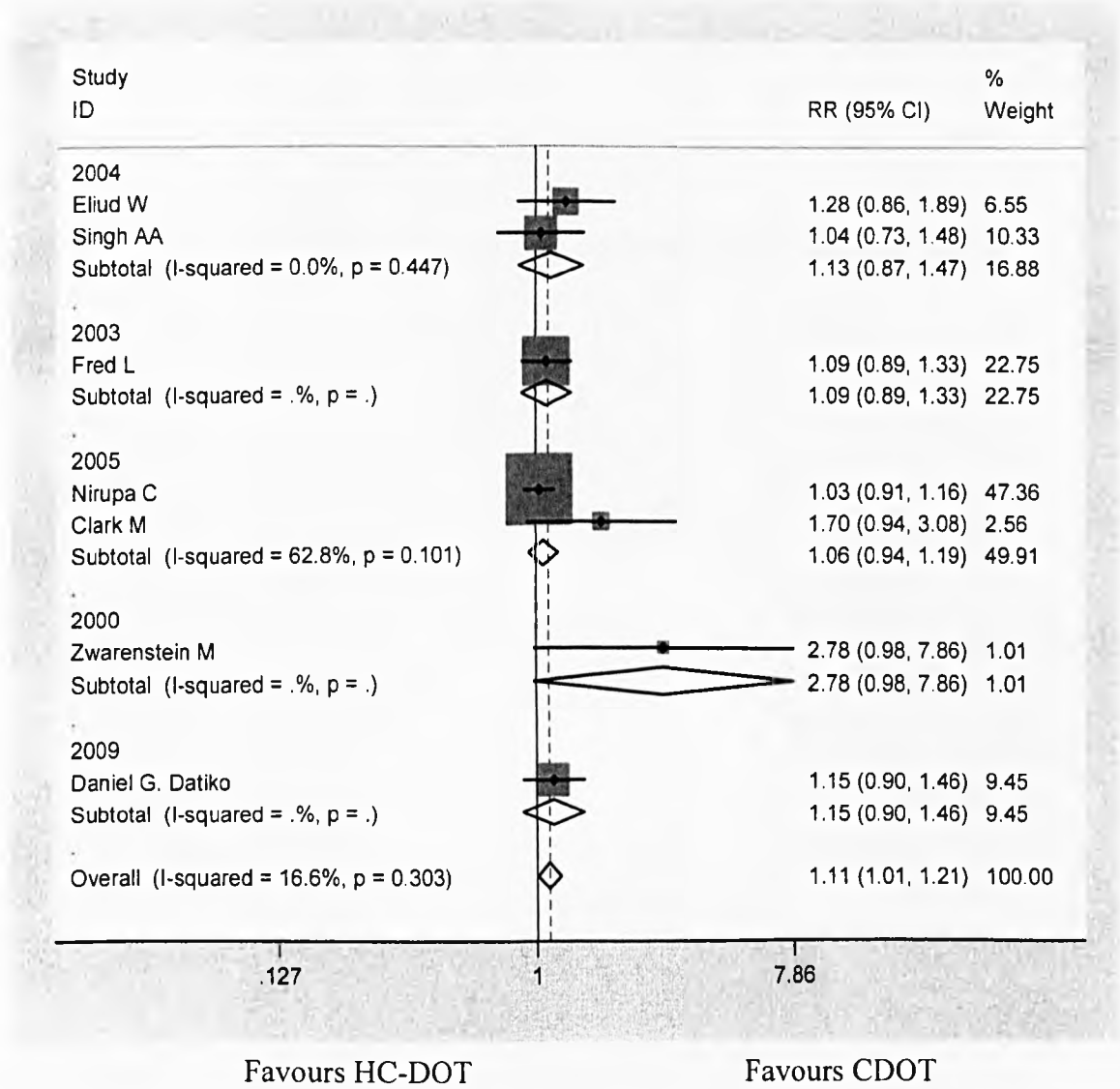


2.9 Exploration of risk of publication bias

2.9.1 RCTs

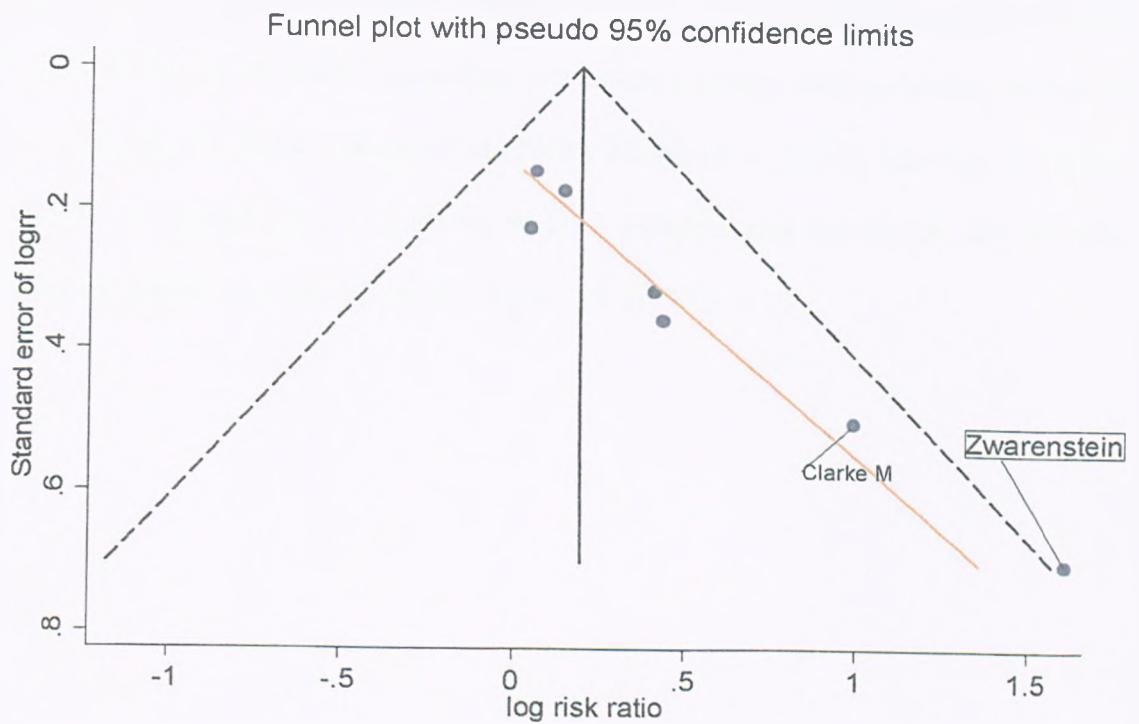
Heterogeneity across the seven studies was not significant ($p=0.303$) (Zwarenstein M 2000; Fred L 2003; Eliud W 2004; Singh A.A 2004; Clarke M 2005; Nirupa C 2005; Daniel G. Datiko 2009); however, as is known, the size of study could affect the treatment estimates. In the forest plot (A.C.Sterne 2009), the confidence-intervals for the studies by Zwarenstein M (2000) and by Clark M (2005) were very wide ($p=2.78$, CI: 0.98-7.86, and $p=1.70$, CI: 0.94-3.08); these studies had small sample sizes compared to the others. (Figure 10 and Figure 11). Figure 10 presents forest plots by the analysis according to the year of study; the smallest studies were conducted in 2000 and 2005 to compare the difference for smear-positive patients between CDOT and HC-DOT (Zwarenstein M 2000; Clarke M 2005), the larger studies were published later in 2003, 2004 and 2009.

Figure 10: Forest plots by year of publication for CDOT versus HC-DOT RCTs



Moreover, the funnel plot test (Figure 11) shows that the standard error for the studies by Zwarenstein M (2000) and by Clark M (2005) is large compared to the others with small sample sizes.

Figure 11: Graph of funnel plots in CDOT versus HC- DOT in RCT studies

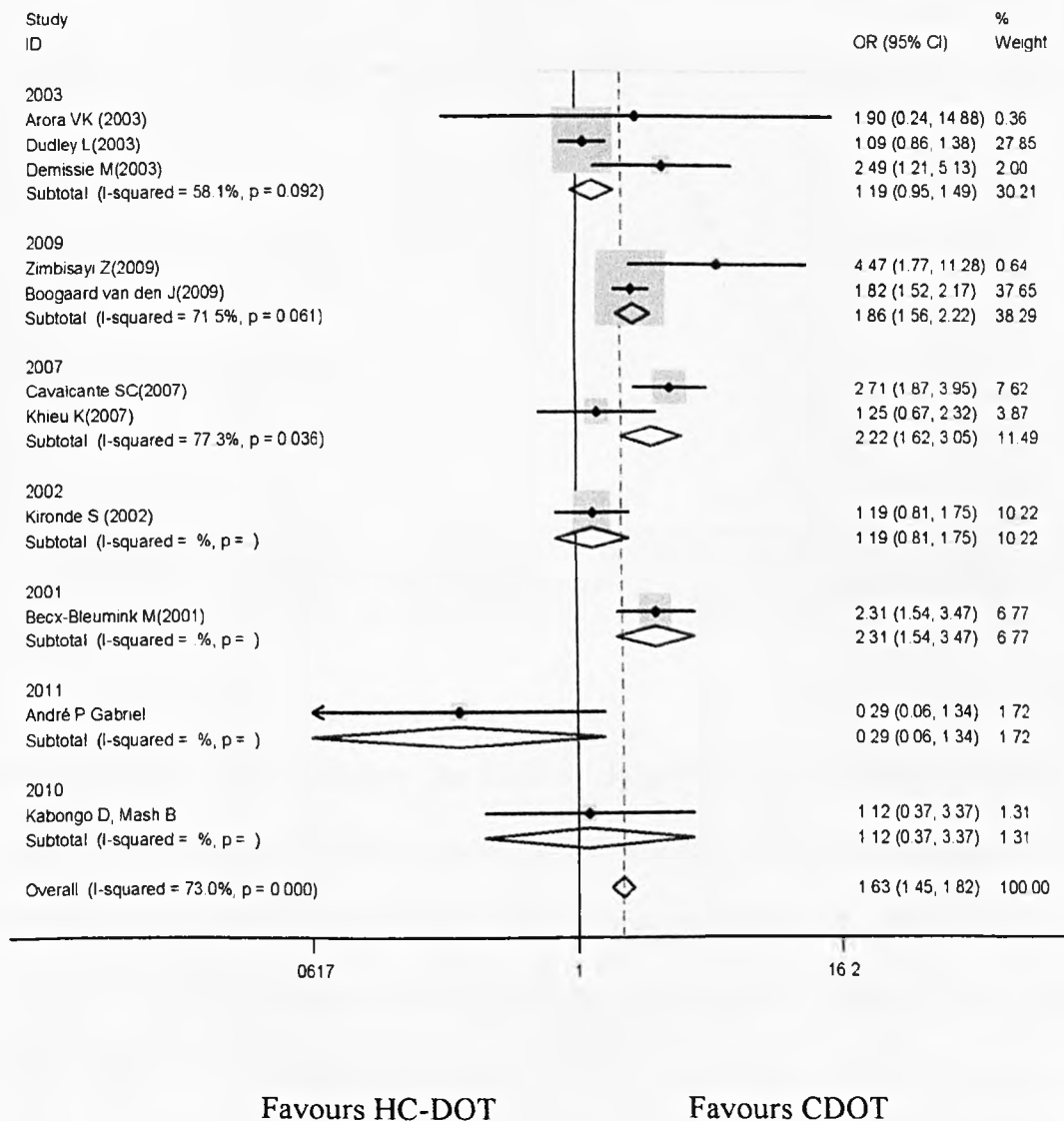


Using Harbord's modified test to analyse the small sample size studies effect in the treatment results for smear-positive in RCTs, the estimated bias coefficient is 2.52 with standard errors of 0.44, giving the p-value 0.002. This shows some evidence of small study bias by Zwarenstein M (2000) and by Clark M (2005) effect on publication bias in the review for RCTs.

2.9.2 Non-RCTs

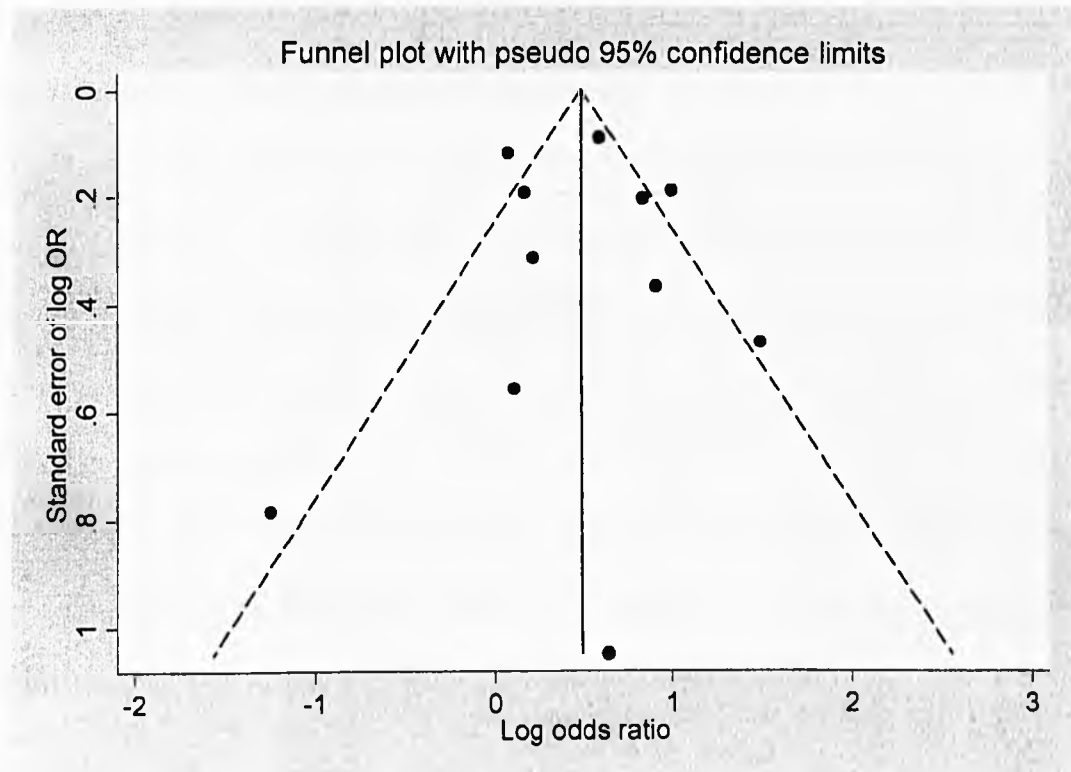
The forest plot for eleven studies (Becx-Bleumink M 2001; Kironde S and Kahirimbanyi 2002; Arora V.K 2003; Demissie M 2003; Dudley L 2003; Cavalcante S.C 2007; Khieu K 2007; Boogaard van den J 2009; Zimbisayi Zvavamwe and Ehlers 2009; Kabongo D and B 2010; André P. Gabriel and Mercado 2011) comparing the treatment outcomes between CDOT and HC-DOT, according to the year of study, the confidence interval of study by Arora VK (2003), Demissie M (2003), Zimbisayi Z (2009), Kabongo D (2010), and André P. Gabriel (2011) were very wide; it indicates that the sample size of these studies was smaller than the others. See Figure 12 and Figure 13.

Figure 12: Forest plots by year of publication in CDOT versus HC- DOT in non-RCTs



The Funnel plot (Figure 13) has also illustrates that the standard error for the studies by Arora VK (2003), Demissie M (2003), Zimbisayi Z (2009), Kabongo D (2010), and André P. Gabriel (2011) were very large because their sample sizes were very small. There appeared to be no association between year of study and study findings.

Figure 13: Funnel plot of studies of CDOT versus HC- DOT in non-RCTs



Using the Harbord test to analyse the small-study effects in the treatment results for smear-positive in non-RCTs studies, the estimated bias coefficient is 0.080 with standard errors of 1.13, giving the p-value 0.945. This suggests no evidence that studies by Arora VK (2003), Demissie M (2003), Zimbisayi Z (2009), and André P. Gabriel (2011) have a significant effect on the results and no evidence publication bias in the review for non-RCTs.

2.9.3 CDOT vs Family DOT

Publication bias and small-study size effects for the four studies (Wright J 2004; Mathew A 2005; Newell JN 2006; Anuwatnonthakate A 2008), comparing the treatment outcomes

between CDOT and family DOT in the review were not tested because the studies were few and combined both RCTs and non-RCTs.

2.10 Summary of the findings and Discussion

The focus of this review is on the effectiveness of CDOT with the alternative DOT options. This review compared the CDOT intervention program separately with HC-DOT and with family DOT, but not with self-administration of treatment. We analysed results separately for RCTs and non-RCTs, rather than reviewing only RCTs. The synthesis of findings from non-RCTs studies in this review has shown a significant difference in treatment success rates for smear-positive TB between CDOT compared to other DOT options. Patients treated under CDOT were significantly better in combined cure and treatment completion rates compared to other DOT options.

The previous reviews by Garner and Volmink (Garner P and Volmink 2000; Garner P and Volmink 2007) which reviewed only eleven studies of RCTs, showed no difference in success rates (cure and treatment completion) for those supervised by community health workers compared with staff at health centres or family members. It was noted in the review that, “there is no evidence that one form of DOT is better than another” (Garner P and Volmink 2000). However there have been several studies published since these reviews which made this updated review necessary.

As we know the RCTs is the most robust study design to determine treatment outcomes between intervention and control groups. The results of the meta-analysis of seven trials shows a borderline statistically significant benefit in treatment success for smear-positive TB patients treated with CDOT compared with HC-DOT (RR=1.05, CI: 1.01-1.10).

However, if we analyse only the five studies with large sample size and eliminate the two small studies, the result shows no statistically significant difference in the treatment success for smear-positive TB between the CDOT and HC-DOT (RR=1.035 CI: 0.99-1.08); this may be due to the lower power to detect a difference. This result is consistent with the earlier review by Garner and Volmink (RR=1.03, CI: 0.96-1.10). As Garner and Volmink noted in their review, the comparison between CDOT and family DOT with HC-DOT did not demonstrate a difference in treatment outcomes. My review also indicates that the effectiveness of CDOT is similar to the HC- DOT or family-DOT, but with the CDOT appearing to maintain somewhat better treatment outcomes, with increased cure or treatment completion.

A review of qualitative evidence by Munro S (Munro S, Lewin. S et al. 2007) reported that adherence to TB treatment depends on patients' access to health facilities, availability of health care providers, distance of the patient's house from the health centre, and availability of transportation. CDOT may be particularly useful in developing countries, where TB caseloads are often overwhelming, the distances to HCs may be substantial and transport facilities limited, and health facility staff and financial resources are limited. As well as achieving at least as good treatment outcomes, CDOT can bring the treatment closer to the patients' homes, enabling patients to continue their normal activities (David W and Geraint 1997; Nirupa C 2005) and feel comfortable with their DOT supporters (Nirupa C 2005). For these reasons, CDOT probably improves patients' treatment adherence.

In additional, several studies of cost-effectiveness of CDOT compared to HC-DOT, not included in the review, have shown that CDOT is less expensive and so more cost-

effective than the HC-DOT (David W and Geraint 1997; Islam AMD 2002; Khan MA 2002). The cost of using community health workers as DOT supporters has been found to be lower than in government facilities for health system (Wandwalo E 2005). CDOT not only reduced costs to the health care system, but also reduced costs to patients. A study by Wandwalo Eliud (Wandwalo E 2005) showed that CDOT reduced costs by 35%, and cost fell by 27% for health services and 72% for patients. The main reason for reduced costs to patients was less number of visits to HCs. The cost per patient successfully treated with CDOT was USD\$128 compared to USD\$203 for HC-DOT patient (Wandwalo E 2005),

Comparing the treatment outcomes between CDOT and family-DOT, there is also evidence that implemented CDOT including family-DOT is still effective and can achieve good treatment success in poor settings with limited resources.

2.11 Limitation of the review

A study of this nature has many limitations. Firstly, there were differences between the studies in terms of which participants were involved. Some studies included only smear-positive TB, while others included all TB forms; in which we extracted the outcomes for smear-positive TB only. The results from this review have shown only the effectiveness of CDOT compared to the other DOT options for smear-positive patients. It may be that the results would be different if we include all TB forms.

Secondly, some of the studies were RCTs, while others were non-RCTs. However, to minimize the impact on the results, RCTs were reviewed and synthesised separately, because the validity of RCTs is better than non-RCTs. Moreover, the results from RCTs

were analyzed by an intention to treat model, while non-RCTs utilized an explanatory model which analyzed outcomes based on the interventions patients actually received and which in some cases they had chosen. This could have introduced the selection bias for non-RCTs because participants were not randomised in these studies and the confounding factors could not control.

Lastly, many of these studies may have been published because they were successful. There may be studies that were not published because they did not show the effectiveness of CDOT; this could introduce some publication bias.

2.12 Conclusion chapter two

Implications for practice

This review synthesises evidence on the effectiveness of CDOT compared to HC-DOT and finds it to be very slightly more effective but similar. CDOT would be useful in rural areas where the infrastructure is very poor; especially where the CDOT may help to increase patients' adherence to treatment. However, it should be also considered how to implement CDOT and who will be the best person to supervise. It is important to note that the CDOT cannot replace the effective health facility in TB control, but can complement the service and contribute to better treatment outcomes.

Implications for research

Further research needs to be conducted to evaluate the effectiveness of CDOT in settings where resources are limited. In particular as treatment for TB is very costly, it is important that more cost effectiveness studies are carried out to indicate, especially for

low income countries, how best to use their scarce resources for TB treatment. In addition, more studies are required to assess the effectiveness of CDOT in other areas where the program has already been implemented such as in Cambodia, to compare the treatment outcomes before and after CDOT implementation; it is especially important to assess the acceptability of implementing CDOT for patients and staff at health facility level.

3 CHAPTER 3: Pilot Study

This chapter describes the pilot study for both the quantitative and qualitative arms of the new study which was conducted as part of this Dr.PH. It includes an assessment of the quality of data and describes any problems which occurred during the pilot study and how they were addressed.

3.1 Purposes of the pilot study

A pilot study of CDOT and HC-DOT in Cambodia was conducted in 2008 after approval from the National Ethics Committee for Health Research in Cambodia. This was done in collaboration with the Cambodian National Tuberculosis Programme (NTP). The main reasons to carry out the pilot study before the main trial were:

- a. To examine the feasibility of extracting data from the existing records such as patients' registered book at the HCs and patients' treatment cards, and check the data quality
- b. To find out the design effect for the quantitative study, and
- c. To pre-test the qualitative study tools, including eliminating or amending questions that did not yield useful information

3.2 Data collection and entry

3.2.1 Data collection for the quantitative study

After receiving the approval from the Cambodian National Committee, quantitative data were collected for the pilot study. Data from the NTP indicated that 108 HCs had implemented CDOT between 2004 to 2007, and 299 HCs implemented the HC-DOT known as ambulatory DOT between 2004 to 2007.

Four HCs were selected for the pilot study; two HCs had implemented CDOT and the other two used HC- DOT. The HC was considered as a large HC if the TB case loads were more than 15 cases per year. In CDOT, one small HC (14 TB cases in 2007) and one large HC (38 cases in 2007) were selected. However, in HC-DOT we could not select a small HC, because these two HCs were large centres (>50 TB cases in 2007).

New smear-positive, negative pulmonary and extra-pulmonary TB patients aged 18 and over were included in the pilot study. Patients treated in 2002, 2003, 2005 and 2006 were identified from the patient register book. 544 patients in total were included in the pilot study.

3.2.2 Data collection for the qualitative study

Topic guides were developed by the author and agreed with the supervisor and in-depth interviews and focus group discussions were conducted to test these topic guides for the qualitative study in order to eliminate questions that did not give information for the study, and to clarify the instructions and the length of time taken for completion of interviews.

Two focus group discussions were conducted among patients who were treated with CDOT and those who were treated with HC-DOT to explore the general issues regarding their treatment experiences under the both DOT options. There were 5 to 6 patients in each group. In-depth interviews were conducted to gather more detailed information about the structure, experiences and patient satisfaction under each DOT approach. Six patients (3 females and 3 males), five male TB staff, and three health volunteers (2 males and 1 female) were selected for the in-depth interviews.

3.2.3 Data description

A Quantitative study

A description of the data collected during the pilot study for the quantitative study is given below. Six research assistants (three nurses and three doctors who were experienced and had been working with NTP and hospitals for at least five years) were recruited and trained by the author for the data collection. Data collection involved visiting the HCs and extracting data from their records.

Table 1: Data collection for the quantitative study

Conceptual variables	Operational variables
Socio-demographic	Sex, age
Examination	Date and year treatment started
Type of TB	BK+, BK-, EP
Referred patient to HC by	Staff, Health volunteer, Family, Neighbour, Others (describe)
Type of patient	New patient, relapsed, defaulter, Transferred-in, multidrug-resistance
Type of DOT	Community-based DOT, Hospital DOT, ambulatory DOT(health centre-DOT), No DOT
Treatment outcomes	Cured, treatment completed, defaulted, failure, died, transferred-out

The checklist included: 1) Socio-demographic, 2) Type of TB, 3) Type of patient, 4) Type of DOT, and 5) Treatment outcomes, for individual patients was translated into the Khmer language. The checklist was developed based on the available information from the health centre's patient register.

B Qualitative study

Interviews were conducted to test the topic guide for the qualitative study for the following reasons: to eliminate questions that did not provide enough relevant information for the study, and to clarify the instructions and the length of time taken for completion of interview.

The interviews were conducted by the author in Khmer language, and took place at the patient's house, the DOT watcher's house and the health centre for staff. Each interview took between 45 minutes to one hour, and two note takers were trained before the interviews. The topic guide for the interviews is shown in Appendix 4 and was translated into the Khmer language.

Patients who had been treated for TB during 2006 were selected for the interviews. TB staff were selected from the staff list. A list of the DOT watchers was provided by the staff and interviewees were randomly selected by the author.

3.2.4 Data entry

The quantitative data were entered and validated in Epi-Info. The statistical package STATA version 10.0 was used to estimate the design effect of treatment success based on combined cure and treatment completion.

The qualitative data were analysed along general themes including choice of treatment, responsibilities of DOT watchers in TB treatment, patients' experiences with DOT treatment, patients' adherence to treatment, people providing patient motivation and support, incentives that patients received during the treatment, and factors influence to

complete the treatment. The emergent categories and subcategories were identified; the relationship between the various categories would be examined to get more detailed information for the results.

3.3 Results of the pilot study

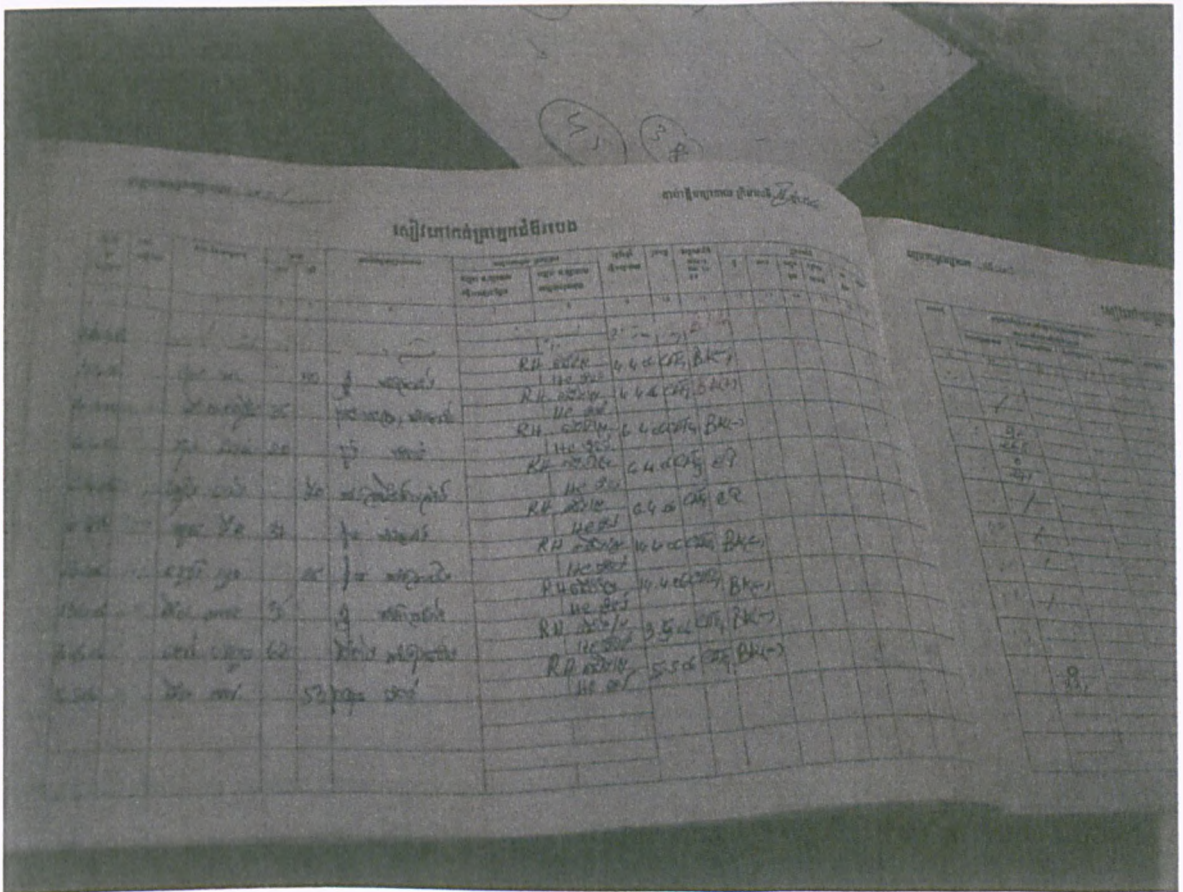
3.3.1 Results of the pilot quantitative study

A. Quality of data

The quality of data in the patients' register at the HC level was not as high as expected. The quality depended on the data management of individual HCs; the data management between 2002 and 2003 was very poor because this was when DOT was first implemented. Approximately 10%-15% of data in 2002 and 2003 were missing from the patients' register but researchers double-checked and supplemented this from patients' treatment cards if they were still kept at the HC. Information on who referred patients to the HC was not recorded.



Picture 3: Peamro Health Center, Prey Veng Province



Picture 4: Patients' register book at the health centre

B. Design effect

The design effect for treatment success from the pilot study was very small. For HC with CDOT, the design effect was 0.06 and 0.36 for HC without CDOT. After the author combined data from both HCs with CDOT and without CDOT, the design effect for treatment success from the pilot study was 0.60.

3.3.2 Results of the pilot qualitative study

A. The HC- DOT

Patients registered with HC-DOT were not 100% treated with the HC-DOT. Two of the three interviewees selected from the HC-DOT were found to be in fact non-DOT because they took medicines at home without anyone watching them. Their families went to collect drugs at the health centre once per week for the first two months and once per month for the rest, as reported from interviews below:

Q: Who was your DOT watcher?

A: I didn't have one....I swallowed medicine at home by myself. I was very sick.

Q: Who went to collect medicines from the health centre for you?

A: My son..but sometimes my wife, she stopped to collect drugs for me after she returned from the market. (Patient, male 55 years old)

"I can't go to the health centre every day. I took medicines with staff only the first two days....then I asked doctor to take medicines at home because I needed to take care of my rice field and my children had to go to school...every morning I was very busy...Then doctor allowed me to take medicines at home..But he told me that I shouldn't tell anybody because it was against the rule. He allowed me to keep medicines at home for 1 week for

the initiate phase...after he believed I took medicines regularly, he let me keep medicines one month” (Patient, female 37 years old).

Patients treated with HC-DOT were required to come to the HC every morning from Monday to Friday. During the weekend or on public holidays, patients were allowed to keep medicines at home. Treatment flexibility was given to patients treated with the HC-DOT.

“We require patients to come to HC for swallowing medicines in front of our staff every morning from 8 to 10 am. However, we give medicines to them during the weekend and holiday. For patients who have to work or are away from home, we will let them keep medicines for as many days as they have asked for....However, we always encourage patients to come to take medicines with our staff every day especially for the first two months because it is a very important period. For the continuous phase, we allow them to take medicines at home for those who live far from the HC or have their own reasons why they can't come here, they just come to collect medicines once per month” (Staff, male 45 years old).

B. The CDOT

Patients took medicines at the DOT watcher's house; except for those who were really sick or disabled. DOT watchers were allowed to keep medicines for one to two weeks for the first phase and for one month for the second phase:

“Normally, I was allowed to keep drugs for one week for the first two months....but it depends, sometimes I ask for two weeks because I don't have time to come collect

medicines at the HC...then doctor agreed...but sometimes when the drug stock in the HC is short...staff don't allow me to keep longer than one week" (DOT watcher, female 39 years old)

"The first two months, it is the most difficult time for patients....staff don't allow me to keep medicines for patients at home longer than 2 weeks. But after two months, I am allowed to refill patients' medicines once every month for 4 months" (DOT watcher, male 42 years old)

The arrangements for collecting medicines from the HC depended on the time available to patients, DOT watchers or staff: *"It depends, sometimes staff come to my house and give me medicines, sometimes I collect them when I go for training at the HC, or when I am busy I ask my patients to go to HC for collecting their medicines."* (DOT watcher, male 52 years old).

Sputum control in the fifth and six months was rarely done for patients treated with CDOT compared to HC-DOT. None of the three patients treated with CDOT had a sputum check before they finished their medicines: *"I didn't have any sputum check before I completed my treatment. Doctor and my DOT watcher didn't tell me"* (Patient, female 55 years old).

"My DOT watcher just told me that I would be cured after I took medicines for 6 months. No one told me to go for the test again" (Patient, male 30 years old).

Visiting patients at home during the treatment by staff at the HC was rarely done, except for patients who lived close to staff's house: *"No one from the health centre came to see*

me during the treatment. If I have any problem, I just asked my DOT watcher” (Patient, female 55 years old).

The choice of DOT watcher was not given to the patient. The choice was made by staff at the HC depending on the availability of DOT watcher either in patient’s commune or patient’s village: *“My DOT watcher was assigned by doctor at the HC. He didn’t live in my village....I used to see him before I started the treatment...but we rarely talked”* (Patient, female 55 years old)

“We don’t allow patients to select their own DOT watcher because it would be difficult for us to organize the work...but as you see our commune isn’t big...So everyone knows each other, even though they live in difference villages” (Staff, male 45 years old)

C. Patient satisfaction

All interviewees reported being satisfied with their treatment. They felt better and continued their work as normal after the treatment. They were also happy because the treatment was free. Patients were very happy about their choice of DOT, especially the non-DOT patients, and the fact that patients were allowed to keep medicines at home instead of going to the HC every day.

The selection of the place where patients needed to take medicines depended on staff at the HC. However, patients treated with HC- DOT complained about the travel time and transportation needed to go to the HC. Encouragement to finish the treatment by family members was very important for patients:

“I am very happy and satisfied for my TB treatment because I feel much better. I am cured now. Before the treatment I couldn’t work, I felt tired and I couldn’t even walk to

the rice field. After I took medicines for 3 months, I could work as normal ...Don't feel tired anymore.....But going to the HC everyday and every morning, was difficult for me. I don't have the transportation, sometimes I needed to walk..it took me 20 minutes; and sometimes I needed to borrow my neighbour's motorbike or bicycle. I wanted to give up...but my wife always encouraged me to go because she doesn't want this disease transmitted to my kids” (Patient, male 39 years old).

D. Role of NGOs in CDOT implementation

Most CDOT was implemented by collaboration between the NTP and international or local NGOs such as: USAID, Japan International Cooperation Agency (JICA), Cambodian Health Committee (CHC), Reproductive and Child Health Alliance (RACHA), Partner for Health and Development (PFHAD), Catholic Relief Service (CRS), Save the Children Australia (SCA), and Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM). Some NGOs have provided incentives such as money or materials to DOT watchers when their patients completed the treatment.

“Our government doesn't have any incentive for community DOT watchers but CHC organization provides US\$4 per one patient to our DOT watcher. This money is given to the DOT watcher at the end of the treatment and I need to make sure that the patient is cured or has completed the treatment by seeing the treatment cards..... If a patient drops the treatment before 6 months, the DOT watcher couldn't receive this money. However, the incentive US\$4 isn't really fixed; it depends on the funding from the CHC. For example, last year the CHC told us that they gave the DOT watcher US\$4 per patient but yesterday I just heard that they will change from US\$4 to US\$2 by the end of this year.”
(Staff, male 45 years old)

Some NGOs have supported the CDOT by providing free health care services to CDOT watchers. *“RACHA doesn't provide any money to our staff or to DOT watchers. But when a DOT watcher's family is delivered a baby in this HC, the hospital fee is free because the RACHA pays the fee.”* (Staff, male 50 years old)

E. Focus group discussion

The focus group discussion could not be done in the pilot study due to two reasons. The first reason was the location; it was very difficult to gather 5 to 6 patients for the interview due to the fact that they do not live in the same village or the same community. The second reason was to do with TB stigmatization; the author found out during the interviews that even though patients understood TB is an infectious disease, they did not want to disclose their disease to anyone else beside their family, as mentioned by patient, female 55 years old below that:

A: I understand that TB isn't a genetic disease but I still didn't want my daughter's fiancée family in-law to know that I took TB medicines, so I asked my DOT watcher not to disclose information to anyone else besides staff at the HC.

Q: Why didn't you want your daughter's fiancée family in-law to know?

A: I wasn't really sure that her fiancée's family in-law understood that TB is an infectious disease.....I was afraid he wouldn't want to marry my daughter anymore.....



Picture 5: The author and research team meeting with patient

3.4 Implication from the pilot study

3.4.1 Quantitative study

According to the results from the pilot study, it was feasible to use a before- and after-study to compare the treatment success between the CDOT and HC-DOT approaches in this research. However, data from the patients' register book were not complete, and the patients' treatment cards needed to be checked for any missing information cases. Due to the facts that between 10% and 15% of data are missing from the register book, the author decided to fill in a 10% missing value for the sample size calculation in the main research.

From several meetings between the author and key TB staff during the pilot study, it emerged that all parties expected that implementation of CDOT would improve the treatment success of smear-positive TB by some 5% compared to the HC-DOT average. This point would be used for the sample size calculation in the research.

Findings from the pilot study showed that not all patients who were registered with CDOT were treated using this approach, but some of these patients were treated with the ambulatory DOT. Similar cases were observed among patients who were registered with HC-DOT. So for the main study, only patients treated with CDOT under the HC-CDOT approach and those patients who were treated with the ambulatory DOT under HC-DOT approach would be selected.

Since there was not sufficient information about patients' referral – i.e. who provided patients' references, the author decided that these data would not be used for the main research.

3.4.2 Qualitative study

The author decided to exclude the focus group discussion from the main research project due to the reasons mentioned above. Since most TB patients had a low-education level, the questions needed to be more specific and more structured. The time for the each interview would take between one hour to one and a half hour depending on individual patient – i.e. how long it will take the patient to understand and answer questions.



Picture 6: Author and research team visited inpatients at Referral hospital



Picture 7: Author, TB doctor and research team during field visited in the community

4 CHAPTER 4: Methodology for the Quantitative Study

The research was developed based on two different methodologies: quantitative and qualitative methods. The quantitative design of this research was a controlled before-after study of the introduction of the CDOT. This chapter presents the objectives and methodology used for the quantitative study.

4.1 General objective

This study aims to examine how the CDOT approach differs from HC-DOT in terms of its implementation in the field and its impact on TB outcomes, including case notification and treatment success in Cambodia.

4.2 Specific objectives

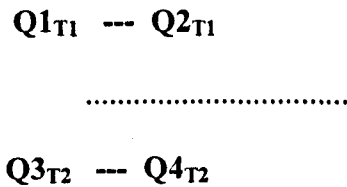
In order to study the difference between CDOT and HC- DOT, the specific objectives of the study are as follows:

- a. To compare the treatment outcomes of the HC- DOT and the CDOT,
- b. To compare the treatment outcomes within the HC before and after implemented CDOT, and
- c. To compare the TB case finding of HC-DOT and the CDOT.

4.3 Methodology

4.3.1 The study design

This study was designed as a controlled before-after implementation of the CDOT as shown in the diagram below:



The baseline for this study was the year 2002-2003 (T1) when CDOT was not yet implemented. In Cambodia, CDOT was introduced in 2004 and fully implemented in some areas in 2005. The quantitative component of this study was used to collect information at baseline (2002-2003, T1) and at two years after CDOT was implemented (2006-2007, T2).

Q1 and **Q3** indicate the random samples selected from HCs where CDOT has been implemented (intervention areas) and **Q2** and **Q4** indicate the random samples from HC-DOT (control areas). **T1** indicates the time of data collection to be the baseline (2002-2003) whereas **T2** indicates the time of data collection at two years after CDOT was implemented (2006-2007). The dashed line indicates that study participants were not randomly assigned to intervention and control groups.

4.3.2 Study outcome measures

The primary outcome measures for the study are the treatment outcomes for smear-positive, smear negative and extra-pulmonary TB patients. The outcome measures used were: “treatment success”, “death”, “defaulter”, “treatment failure” and “transferred out”. “Treatment success” was combined between cured and treatment completion. Cured patients were defined as those who were sputum smear-positive before starting treatment and were confirmed sputum-negative at five (or 6) months on at least one occasion. Treatment completion was defined as completion of the full course of treatment but no sputum taken at the end of treatment. Patients, who remained or became smear positive at five (or 6) month or later during treatment, were classified as “treatment failures”. Patients who died during the treatment due to TB disease or other cause, were recorded in the “death” group. “Defaulter” refers to patients who failed to collect drugs for more than two consecutive months during treatment. “Transferred out” describes patients who transferred to another health centre region.

The secondary outcome was the percentage of TB case finding by year from 2002 until 2008 in both groups. According to the NTP, case finding is defined as TB suspects who had a cough for more than two weeks, and were referred for a sputum test at the HC.

4.3.3 Study sites

HCs which had implemented CDOT over the whole period 2005-2007; were eligible for selection for the CDOT group. In contrast, HCs which had only applied regular ambulatory DOT since 2004 were eligible to be chosen for the HC-DOT group.

The NTP report in 2007(NTP 2007), indicated that there were 227 HCs implementing CDOT in 2005; in 41 HCs CDOT was withdrawn in 2005 due to lack of funding from the NGOs, such as PFHAD, SCA, CRS, RACHA, who had supported the CDOT program. Because one province was very difficult to access by road, it was not included in the study. In total, 186 HCs within 11 provinces and 21 ODs were eligible for selection for the CDOT group.

Between 2004 and 2007, there were 285 HCs within 13 provinces which had not implemented CDOT, of these 6 HCs were located in 2 provinces where the infrastructure was very difficult to access, especially during the data collection period. The researcher therefore decided to exclude those HCs from the study, so 279 HCs in 11 provinces and 32 ODs were eligible for selection for the HC-DOT group.

4.3.4 Study population

The eligible study population was patients 18 years old and over who were registered for treatment in HCs in areas where CDOT was implemented and in areas where it was not, during the period from 1st January 2006 until 31st December 2007, and baseline patients registered in 2002-2003.

New smear positive and smear negative pulmonary tuberculosis as well as extra-pulmonary tuberculosis patients were included in the study. Patients who had been previously treated for TB and patients with multi-drug resistance were excluded because these groups of patients are required to stay in the hospital for treatment.

4.3.5 Description of CDOT

The patients in the CDOT selected health centres had been supervised by a DOT watcher. There are two categories of DOT watchers: 1) member of the village health support group (VHSG); and 2) other community volunteers such as neighbours, former TB patients, school teachers and traditional healers. According to the NTP strategy planning reports, family members are not used as DOT watchers in Cambodia.

4.3.6 Description of HC-DOT

Patients who had received regular ambulatory DOT at HCs were selected for the HC-DOT. Based on the NTP strategy planning, patients treated with HC-DOT have to come to HCs every morning during the two months intensive phase to be observed swallowing the medication by staff at HCs. During the continuation phase of four months, patients are required to come to collect the drug once per week and for clinical evaluation in months 2, 5 and 6.

Patients who had taken medicines at home without any supervisor were excluded from the study because those patients were considered as non-DOT.

4.3.7 Sample size calculation

From the pilot and baseline assessment, the author assumed that CDOT would improve the treatment success of smear positive pulmonary TB patients by 5% compared to the HC-DOT. The sample size calculation, assumed 10% missing values, 25 patients per HC, a design effect of the pilot study was 0.60 and a 5% significant level, we needed 27 HCs for CDOT and 27 HCs for HC-DOT. We identified approximately 1350 participants for

the baseline and another 1350 at two years after CDOT was implemented. The details of the sample size calculations are given in Appendix 5.

4.3.8 Sampling

A. Sampling for the HC

Based on the TB case notification (2006-2007), HCs which had fewer than 50 TB cases for two years (2006-2007) were combined with other HCs in the same operational district and within the same province to create one cluster, as those HCs have similar geography and share the same OD supervisor. In total, we needed 27 clusters from the HCs where CDOT was implemented and 27 clusters from the HC-DOT. Appendix 6 shows the flow of selection clusters of HCs in the study. Appendix 7 shows the list of provinces and HCs selected into the study.

B. Sampling of patients

The selection of representative patients from each HC was done in four stages. For the CDOT, at the first stage patients treated with the CDOT were identified; those patients were counted and listed. The second stage selected a number "A" by calculating N/n where N = total number of patients treated in the HC, and n = number of CDOT patients to be selected as representing the HC (25 patients for each HC). The third stage involved selecting a random number "B" which was less than or equal to "A". The patient in that "B" place on the list would be the first representative patient of that HC in the study. The next patient was selected as the patient in the position "A+B" on the list (eg. $A+B=C$: second patient, $C+A=D$: third patient.....= n), we continued with the same method until we got the total number of patients "n" that we needed in the HC.

For the HC-DOT, we used the same strategy to select representative patients.

To ensure a sample size large enough to calculate reliable estimates for all the desired elements of the study, it was necessary to control the total number of patients drawn per cluster. This was done by selecting 25 patients in every cluster. However, for clusters which had more than one HC, we denoted the larger HC “A”, the medium “B” and the smaller HC “C”. Then we selected 9 representative patients from the large, 8 from the medium and the other 8 patients from the small HC.

4.4 Field preparation

Training took place before the research started (Table 2). The author was responsible for gaining access to HCs, recruitment and training of research assistants, making schedules with staff at ODs and heads of HCs, arrangement of work and travelling schedule, double checking all questionnaires, and analysis of all data.

Table 2: Field preparation for the quantitative study

Activity	Participants	Purpose	Duration
Meeting	<ul style="list-style-type: none">● Director of the NTP● Medical officers of Health in the NTP● Coordinators of TB team at ODs level● The Author● Two Research Assistants	Briefing by the author on the purpose of the research and the research protocol	1 day
Phone call	<ul style="list-style-type: none">● Author● Two Research Assistants	<ul style="list-style-type: none">● Confirming about DOT implemented in HCs included in the study● Briefing on the purpose of the research to ODs level	4 days
Meeting	<ul style="list-style-type: none">● The Author● Head of the ODs● Two Research Assistants	<ul style="list-style-type: none">● Informing and briefing by the author on the purpose of the research● Checking the record books and treatment cards available in the ODs level	3 days
Training	<ul style="list-style-type: none">● The Author● Ten Research Assistants● One Note taker for the qualitative study	<ul style="list-style-type: none">● Collecting technique● Questionnaire forms● Data entry	4 days

Ten research assistants, seven medical doctors and three nurses from the NTP, were employed part time for this study. They were familiar with the TB treatment and DOT information. They were responsible for collecting and completing data schedules of information on participants including sex, type of TB, type of DOT and treatment results for the baseline (2002-2003) and two years after CDOT was implemented (2006-2007). They also checked data from patients' treatment cards when information was missing from the TB register. The researcher was with them in almost all HCs to supervise them throughout the study period. The descriptions of data collected are given in Appendix 8.

4.5 Data collection for TB case-finding

The research assistants also collected information for TB case-finding from the patient register by identifying all new cases including smear-positive TB, smear-negative TB, and extra-pulmonary TB from year 2002 to 2008 in every HC selected in the study. Appendix 9 describes the data for TB case finding.

4.6 Data processing and analysis

4.6.1 Data processing

All completed questionnaires were checked by the author and two main medical doctors (research assistants) at the end of each day to ensure completeness. Incomplete answers were considered as missing data. The information was coded and entered using Epi Data (Laurit Sen JM and M. 2003) by a statistician from the National Institute of Statistics. Data entry began as soon as the field work was finished. Re-entry data was double-checked by one doctor from the National Institute of Public Health, supervised by the author.

4.6.2 Data analysis

Treatment outcomes

The author used STATA version 10.0 (College Station, TX) to analyse the treatment success data. Cluster effects and sampling weights were taken into account where appropriate. First baseline characteristics including age, TB types and treatment success were compared between groups and within groups over time, using chi-square test. The difference between both groups by gender at the baseline was also analyzed using a t-test. Logistic regressions were used to compare treatment success between the two groups and within the two groups over time controlling for age, sex, TB type and residence. Odds ratios and 95% confidence intervals are reported.

Case-finding

The total number of TB cases from 52 CDOT and HC-DOT reported since 2002 to 2008 is included in the analysis. First the annual total of TB cases from 26 HCs implemented CDOT was calculated and compared with the annual total of TB cases from the 26 HCs-DOT. Then two regression lines were used to fit trends of annual total TB cases from 2002 to 2008.

In order to compare the two regression lines, the difference-in-differences method is used (Imbens 2005). All cases reported are tagged with a variable called "post". The author used post=0 to denote the pre-period before CDOT was implemented from 2002-2004 and post=1 to denote the period after CDOT implemented 2005-2008. The outcome is total number of TB cases reported. The "treatment" variable is a model variable. The difference in differences estimator is the estimate of the coefficient on the interaction between the "post" and "treatment" (Larsen February 12, 2008).

4.7 Ethics procedures

All study protocols, consent forms and questionnaires were submitted, reviewed and approved by the London School Hygiene and Tropical Medicine ethics committee and the National Ethics Committee for Health Research in Cambodia before the research started. The baseline and follow-up study of the “evaluation of the effects of CDOT compared to HC-DOT” were approved by the Cambodia National Ethics Committee for Health Research, Ministry of Health and the Boards of National Tuberculosis for TB control Program. The anonymity of all participants approached in the study was guaranteed. It was ensured that there was no names of study subjects are shown in the results. The questionnaire sheets were locked in a safe place.

4.8 Resources and time frame

This research was funded from personal resources and A&H Fujimoto Foundation (private Japanese family fund), which covered expenditure for salaries, transportation, food and accommodation for the research assistants. The research project was supported by the team from CENAT, staff at the ODs level and as well as from the HCs levels. The field work took place from January to July 2009.



Picture 8: Author with research assistance team: collecting data from the registration book at the HC

5 CHAPTER 5: Results of the Quantitative Study

This chapter presents the quantitative results of the study and compares treatment outcomes and TB case finding between CDOT and HC-DOT.

5.1 Participation and distribution

1067 participants were surveyed at baseline in 2002/3 (543 CDOT and 524 HC-DOT) and 1297(655 CDOT and 642 HC-DOT) at two years after the intervention in 2006/7. In total 48 HCs were selected in the CDOT and 34 HCs in the HC-DOT areas.

5.2 Socio-demographic characteristics

The author classified ages into three categories (18-39, 40-59, and ≥ 60). Table 3 presents the distribution of patient characteristics at the baseline assessment and two years after CDOT implementation. Both CDOT and HC-DOT populations were similar with respect to sex distribution at baseline (50.28% vs 50.19% male, 49.72% vs 49.81 female, $p=0.97$) and two years after CDOT was implemented (50.08% vs 46.73% male, 49.92% vs 53.27% female, $p=0.30$). The age distribution did not differ significantly in the two groups ($p=0.47$ for the baseline and $p=0.69$ two years after the CDOT was implemented).

The majority of TB patients in both domains were new smear-positive pulmonary TB patients. At baseline TB types were similar ($p=0.19$) in both HCs; however, after two years the percentage of smear-positive TB patients was higher in HC-DOT (74.45%) than in CDOT (64.12%) patients ($p=0.03$) and the percentage of smear-negative TB cases was lower in HC-DOT (13.08%) compared to CDOT (24.12%). The number of smear-

negatives increased, particularly for CDOT. No statistically significant difference was found for residence.

Table 3: Characteristics of patients at the baseline 2002/3 and at two years after CDOT implemented 2006/7

Characteristic	Baseline assessment 2002/3			2-years after CDOT implemented 2006/7			
	CDOT n (%)	HC- DOT n (%)	Total n (%)	CDOT n (%)	HC- DOT n (%)	Total n (%)	
Sex							
Male	273 (50.28)	263 (50.19)	536 (50.23)	328 (50.08)	300 (46.73)	628 (48.42)	
Female	270 (49.72)	261 (49.81)	531 (49.77)	327 (49.92)	342 (53.27)	669 (51.58)	
p-value				0.97			0.30
Age group							
18-39	175 (32.23)	171 (32.63)	346 (32.43)	208 (31.76)	221 (34.42)	429 (33.08)	
40-59	238 (43.83)	218 (41.60)	456 (42.74)	267 (40.76)	264 (41.12)	531 (40.94)	
60>=0	130 (23.94)	135 (25.76)	265 (24.84)	180 (27.48)	157 (24.45)	337 (25.98)	
p-value				0.47			0.69
TB type							
Smear- Positive TB	460 (84.71)	411 (78.44)	871 (81.63)	420 (64.12)	478 (74.45)	898 (69.24)	
Smear	59	62	121	158	84	242	

	Negative TB	(10.87)	(11.83)	(11.34)		(24.12)	(13.08)	(18.66)	
	Extra-pulmonary TB	24 (4.42)	51 (9.73)	75 (7.03)		77 (11.76)	80 (12.46)	157 (12.10)	
	p-value				0.19				0.03
Residence									
	Banteay Mean Chey	31 (5.71)	-	31 (2.91)		50 (7.63)	-	50 (3.86)	
	Battambang	75 (13.81)	24 (4.58)	99 (9.28)		75 (11.45)	25 (3.89)	100 (7.71)	
	Kampong cham	68 (12.52)	74 (14.12)	142 (13.31)		124 (18.93)	100 (15.58)	224 (17.27)	
	Kampong Chhang	50 (9.21)	49 (9.35)	99 (9.28)		50 (7.63)	50 (7.79)	100 (7.71)	
	Kampong Speu	75 (13.81)	-	75 (7.03)		75 (11.45)	-	75 (5.78)	
	Kampong Thom	-	50 (9.54)	50 (4.69)		-	50 (7.79)	50 (3.86)	
	Kampot	25 (4.6)	-	25 (2.34)		25 (3.82)	-	25 (1.93)	
	Kandal	-	102 (19.47)	102 (9.56)		-	142 (22.12)	142 (10.95)	
	Kratie	19 (3.5)	-	19 (1.78)		31 (4.73)	-	31 (2.39)	
	Phnom Penh	-	25 (4.77)	25 (2.34)		-	25 (3.89)	25 (1.93)	

Prey Veng	-	158 (30.15)	158 (14.81)	-	200 (31.15)	200 (15.42)
Pursat	25 (4.6)	-		25 (3.82)	-	25 (1.93)
Siemreap	50 (9.21)	17 (3.24)		75 (11.45)	25 (3.89)	100 (7.71)
Sihanouk Ville	-	25 (4.77)		-	25 (3.89)	25 (1.93)
Takeo	125 (23.02)	-		125 (19.08)	-	125 (9.64)

5.3 Effectiveness of CDOT

5.3.1 Comparison of treatment outcomes at baseline between CDOT and HC-DOT in year 2002-2003

At baseline, data for 550 and 524 patients were collected from CDOT and HC-DOT areas respectively. After adjusting for sex, age group and TB types, treatment success was similar between CDOT and HC-DOT areas (OR=0.54, 95%CI: 0.27-1.08, p=0.08). The treatment success, defined as combination of cure and completion, was successful and above 90% for all TB types in both areas (CDOT: 94.29%, HC- DOT: 96.76%). There was no statistically significant difference between groups for death or default rates (p=0.22 for the death and p=0.91 for defaulter). The results are shown in Table 4.

Table 4: Comparison of treatment outcomes among all TB patients by type of DOT in year 2002-2003

Treatment outcome	Baseline assessment (2002-2003)							
	CDOT		HC-DOT		Crude OR	Adj OR**	95% CI	p-value
	No.	%	No.	%				
Success*	512	94.29	507	96.76	0.55	0.54	0.27-1.08	0.08
Died	17	3.13	11	2.1	1.51	1.65	0.72-3.76	0.22
Defaulter	7	1.29	6	1.15	1.13	1.06	0.36-3.07	0.91
Failure	3	0.55	0	-	-	-		
Transfer out	4	0.74	0	-	-	-		

*Success is defined as combination of completion and cure

** Odds ratio adjusted for sex, age group and TB type

The odds of a successful treatment outcome for new-smear positive in both areas was also similar at baseline (OR=0.54, 95%CI: 0.24-1.18, p=0.12). There was no statistically significant difference in death rate (OR=1.58, 95%CI: 0.56-4.41, p=0.38) or default rate

(OR=1.06, 95%CI: 0.36-3.06, p=0.91) among smear positive patients between the two areas. Table 5 compares treatment outcomes among new-smear positive TB by type of DOT at baseline.

Table 5: Comparison of treatment outcomes among new-smear positive TB by type of DOT in year 2002-2003

Treatment outcome	Baseline assessment (2002-2003)							
	CDOT		HC-DOT		Crude OR	Adj OR**	95% CI	p-value
	No.	%	No.	%				
Success*	434	94.35	398	96.84	0.55	0.54	0.24-1.18	0.12
Died	12	2.61	7	1.70	1.54	1.58	0.56-4.41	0.38
Defaulter	7	1.52	6	1.46	1.04	1.06	0.36-3.06	0.91
Failure	3	0.65	0	-	-	-	-	-
Transfer out	4	0.87	0	-	-	-	-	-

*Success is defined as combination of completion and cure

** Odds ratio adjusted for sex, and age group

5.3.2 Comparison of treatment outcomes between CDOT and HC-DOT in year 2006-2007

655 and 642 patients for CDOT and HC-DOT areas were recruited in 2006-2007 two years after CDOT was implemented. No statistically significant difference was found for the treatment success rates between CDOT and HC-DOT areas (OR=1.26, 95%CI: 0.56-2.82, p=0.56). The treatment outcome was still very successful in both areas (97.1% for CDOT and 96.57% for HC-DOT). The death and defaulter rates were also similar (p=0.13 for death and p=0.37 for default). See Table 6.

Table 6: Comparison of treatment outcomes among all TB patients by type of DOT in year 2006-2007

Treatment outcome	Two years after the intervention (2006-2007)							
	CDOT		HC-DOT		Crude OR	Adj OR**	95% CI	p-value
	No.	%	No.	%				
Success*	636	97.1	620	96.57	1.19	1.26	0.56-2.82	0.56
Died	10	1.53	17	2.65	0.57	0.50	0.21-1.24	0.13
Defaulter	6	0.92	3	0.47	1.96	1.94	0.44-8.61	0.37
Failure	0	-	1	0.16	-	-	-	-
Transfer out	3	0.46	1	0.16	2.95	3.36	0.34-33.43	0.29

*Success is defined as combination of completion and cure

** Odds ratio adjusted for sex, age group and TB type

Comparing only new-smear positive TB, at two-years after CDOT was implemented, there was a borderline statistically significant difference in death rates in CDOT areas compared to HC- DOT areas after adjusting for sex and age (OR=0.33, 95%CI: 0.11-0.99, p=0.05). However, the overall treatment success for smear positive did not differ between areas (OR=1.21, 95%CI: 0.51-2.86, p=0.66) (Table 7).

Table 7: Comparison of treatment outcomes among new-smear positive TB patients by type of DOT in year 2006-2007

Treatment outcome	Two years after the intervention (2006-2007)							
	CDOT		HC-DOT		Crude OR	Adj OR**	95% CI	p-value
	No.	%	No.	%				
Success*	408	97.14	462	96.65	1.18	1.21	0.51-2.86	0.66
Died	4	0.95	13	2.72	0.34	0.33	0.11-0.99	0.05
Defaulter	5	1.19	1	0.21	5.74	5.75	0.59-55.71	0.13
Failure	0	-	1	0.21	-	-	-	-
Transfer out	3	0.71	1	0.21	3.43	3.36	0.34-33.43	0.29

*Success is defined as combination of completion and cure

** Odds ratio adjusted for sex, and age group

5.3.3 Comparison of treatment outcomes in CDOT areas by year of assessment

Comparing treatment outcomes for the same CDOT areas over time, after adjusting for sex, age, and TB types, there was some evidence of a small non-significant improvement in the treatment success rates from baseline to two-years after CDOT was implemented

(OR=2.10, 95%CI: 0.95-4.62, p=0.06). Moreover, there was a statistically significant decline in death rate among all TB patients at two years after implementation of CDOT compared with the baseline (OR=0.37, 95%CI: 0.15-0.92, p=0.03) (Table 8).

Table 8: Comparison of treatment outcomes for all TB types in CDOT areas at the baseline and two-years after CDOT was implemented

Treatment outcome	CDOT areas							
	Baseline (2002-2003)		2-years after CDOT implemented (2006-2007)		Crude OR	Adj OR**	95% CI	p-value
	No.	%	No.	%				
Success*	512	94.29	636	97.1	2.03	2.10	0.95-4.62	0.06
Died	17	3.13	10	1.53	0.48	0.37	0.15-0.92	0.03
Defaulter	7	1.29	6	0.92	0.71	0.86	0.29-2.53	0.79
Failure	3	0.55	0	-	-	-	-	-
Transfer out	4	0.74	3	0.46	0.62	0.83	0.19-3.56	0.80

*Success is defined as combination of complete and cured

** Odds ratio adjusted for sex, age group and TB type

No statistically significant difference was found for treatment success rates for smear positive patients when analysed by CDOT areas before and after the intervention (OR=

2.07, 95%CI: 0.86-4.99, p=0.10). However, there was a non-significant decrease in the death rate for smear positive TB at two year after CDOT was implemented compared with the baseline (OR=0.35, 95%CI: 0.10-1.12, p=0.08) (Table 9)

Table 9: Comparison of treatment outcomes for new-smear positive TB patients in CDOT areas at the baseline and two-years after CDOT was implemented

Treatment outcome	CDOT areas							
	Baseline 2002-2003		Two-years after CDOT implemented 2006-2007		Crude OR	Adj OR**	95% CI	p-value
	No.	%	No.	%				
Success*	434	94.35	408	97.14	2.04	2.07	0.86-4.99	0.10
Died	12	2.61	4	0.95	0.36	0.35	0.10-1.12	0.08
Defaulter	7	1.52	5	1.19	0.78	0.77	0.24-2.49	0.66
Failure	3	0.65	0	-	-	-	-	-
Transferred out	4	0.87	3	0.71	0.82	0.83	0.19-3.56	0.80

*Success is defined as combination of completion and cure

** Odds ratio adjusted for sex, and age group

5.3.4 Comparison of treatment outcomes in HC-DOT areas by year of assessment

After adjusting for sex, age, and TB types, in HCs which implemented ambulatory DOT, there was no statistically significant improvement in treatment success (OR=0.90, 95%CI: 0.45-1.81, p=0.77) or death rate (OR=1.35, 95%CI: 0.59-3.08, p=0.46). Table 10 shows the result.

Table 10: Comparison of treatment outcomes for all TB types in HC-DOT areas at the baseline and two-years after the CDOT intervention

Treatment outcome	HC-DOT areas							
	Baseline 2002-2003		2-years after the CDOT intervention 2006-2007		Crude OR	Adj OR**	95% CI	P-value
	No.	%	No.	%				
Success*	507	96.76	620	96.57	0.94	0.90	0.45-1.81	0.77
Died	11	2.1	17	2.65	1.27	1.35	0.59-3.08	0.46
Defaulter	6	1.15	3	0.47	0.40	0.40	0.1-1.59	0.19
Failure	0	-	1	0.16	-	-	-	-
Transfer out	0	-	1	0.16	-	-	-	-

*Success is defined as combination of completion and cure

** Odds ratio adjusted for sex, age group and TB type

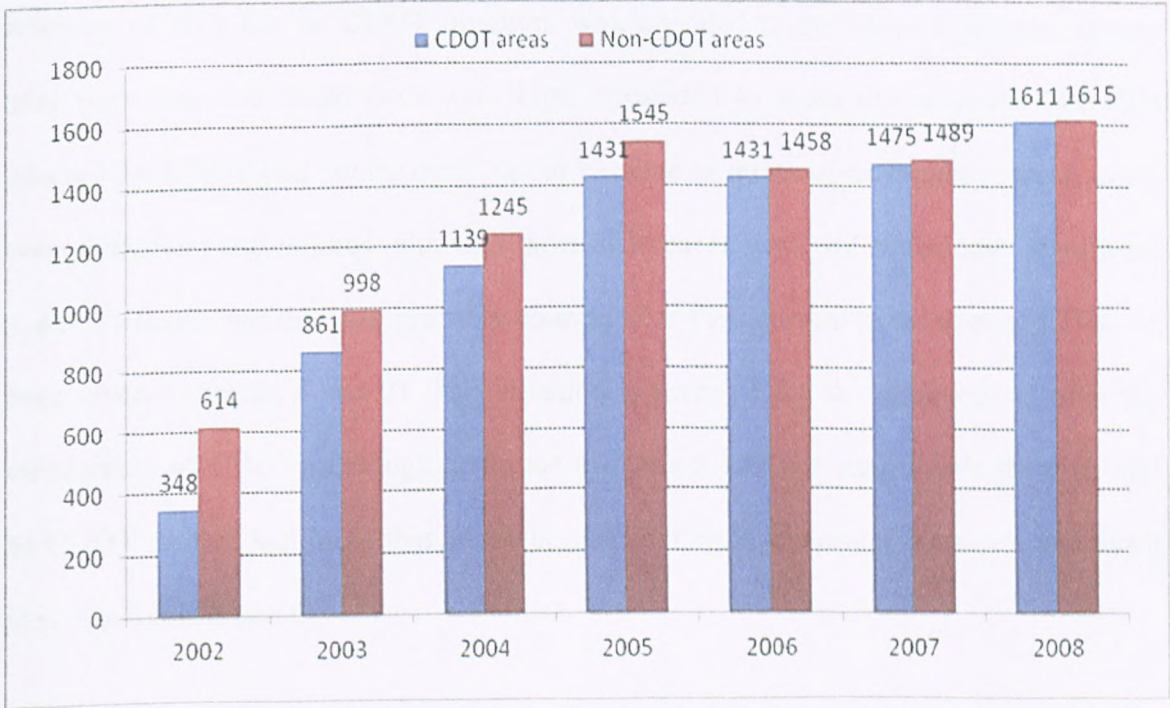
5.4 TB case-finding

Most of the patients registered in both CDOT and HC-DOT areas were new smear-positive TB cases. At baseline (2002-2004) in the CDOT HCs, TB case-finding was very low at 348 cases in 2002, 861 cases in 2003 and 1139 cases in 2004 compared to the HC-DOT 614 cases in 2002, 998 cases in 2003 and 1245 cases in 2004. The average case finding rates under CDOT and HC-DOT areas were 25 and 30 patients respectively per year. After CDOT was implemented in 2004, TB case-finding continued to increase dramatically from 1431 cases in 2005 to 1611 cases in 2008. TB case-finding in HCs without implemented CDOT also increased, but the trend was much less from 1545 cases in 2005 to 1615 cases in 2008. Table 11 shows the total TB case-finding from 2002 to 2008. Figure 14 illustrates the TB case-finding rate by year for both CDOT and HC-DOT areas.

Table 11: Number of total TB case-finding by HCs- CDOT and HCs-DOT from 2002-2008

	Year of reporting						
	2002	2003	2004	2005	2006	2007	2008
HCs with CDOT	348	861	1139	1431	1431	1475	1611
HCs-DOT areas	614	998	1245	1545	1458	1489	1615

Figure 14: TB case-finding by year under both HCs with CDOT and without CDOT, 2002-2008



However, further analysis of TB case-finding by using the difference-in-differences method shows that TB case-finding from HC with CDOT implemented and HC-DOT over time was equal. The TB case-finding between these two HCs was not significantly different (p-value: 0.547). This test shows that even though the trend of TB case-finding is seen to increase after the implementation of CDOT, the slopes were not significantly different.

5.5 Summary: key findings from the quantitative study

CDOT tended to maintain high treatment success rates (97.1%) as did HC-DOT (96.57%) with no significant difference between them (OR=1.26, 95%CI: 0.56-2.82, p=0.56). A key finding of this study is that in CDOT areas, treatment success rates tended to show

small non-significant improvements in treatment success rates from baseline to two-years after implementation (OR=2.10, 95%CI: 0.95-4.62, p=0.06). Death rates were significantly reduced (OR=0.37, 95%CI: 0.15-0.92, p=0.03). This difference reflects the selection of HCs for the CDOT program, which tended to be where treatment success rates were low and death rates were high, compared to areas not selected. The HCs selected for CDOT had poorer outcomes at baseline in terms of treatment success, death rates, defaulters and failures (although these differences were not statistically significant at the 5% level) and this was probably connected to the decision to implement CDOT in these centres (Tables 6 and 7). This situation is reversed for the comparisons after the introduction of CDOT (although again the differences are not significant) showing that the CDOT centres had more than made up their deficit in treatment outcomes and death rates (see Table 8 and 9).

The trend of TB case-finding at HCs with CDOT showed a dramatic increase overtime after the CDOT implementation, although not statistically significantly better than TB case-finding at HC-DOT (p=0.547) (Figure 14). However the further analysis of TB case-finding by using difference-in-differences method, shows that TB case finding from HC with CDOT implemented and HC-DOT over time were equal. The TB case-finding between these two HC groups was not statistically different (p=0.547). This test shows that even though the trend of TB case-finding is seen to increase after the implementation of CDOT, the slopes of increase were not significantly different.

6 CHAPTER 6: Qualitative Methods

This chapter presents the methods of the qualitative study which aimed to explore the experiences of both CDOT and HC-DOT among patients, staff and DOT watchers.

6.1 Objectives

The specific objectives of study are:

- a. To explore how HC-DOT and CDOT are functioning
- b. To determine the strengths and weaknesses for each approach, and
- c. To assess the acceptability of CDOT and HC-DOT to HC staff, TB patients and DOT watchers

6.2 Study population

Patients treated for TB in 2007 in both types of HCs included in the quantitative study were selected for the interviews. DOT watchers and health workers, who had experience supervising or watching patients taking medicines, were also interviewed, as were selected staff working at the TB section.

6.3 Methodology

The methods used were a combination of in-depth interviews and observations of new patients who were treated in 2009 and had taken medicines in the HCs and in the community with DOT watchers. In addition, the informal conversations between the

author and patients or their families relating to the experiences of TB treatment were also noted for the analysis.

6.3.1 Sampling methods

In the qualitative study only two age categories were used, “young people” were defined as those between 18 to 40 years old because they were of reproductive ages. Those aged over 40 years were categorized as “old”.

Purposive sampling in qualitative research aims to find information rich cases (Patton 2002), with a mixture of typical, extreme and political sampling. An “extreme” case would be someone who was very old, and a “typical” case would be a patient from a rural setting or an urban area. “Political sampling” would be of someone who was very old and from a very deprived area with known problems of access. Table 12 shows the sampling matrix for the purposive sampling used in the study, sampling by rural and urban setting, gender and age.

Table 12: Sampling matrix for identified interviewee

Interviewee	Location		Gender			
	Rural	Urban	Male		Female	
			≤40 years	>40 years	≤40 years	>40 years
	Patients	43	8	7	15	13
DOT watchers	18	0	2	10	2	4
Heath staff	21	6	13	11	2	1

Patients were randomly selected by the author based on the sampling matrix stratification through the quantitative list. DOT watchers were identified through staff recommendation or were selected by the author. HC staff were selected for interview based on their TB job experience and their availability during the presence of the author. Methods and criteria for eligibility are shown in Table 13.

Table 13: Methods and criteria included for the interviews

Interviewee	Methods	Criteria for eligibility
Patients	<ul style="list-style-type: none"> ● In-depth interviews ● Observation taken of new patients treated in 2009 	<ul style="list-style-type: none"> ● Smear positive, smear negative and extra pulmonary TB ● Treated for TB with CDOT and the ambulatory DOT in 2007 ● Included in the quantitative study ● Cured, completed and defaulter patients
DOT watchers	<ul style="list-style-type: none"> ● In-depth interviews ● Observation during distributed and supervised medicines to patients for current patients 	<ul style="list-style-type: none"> ● Experiences in distributing and watching patients taking medicines
Health staff	<ul style="list-style-type: none"> ● In-depth interviews ● Observation during distributed and supervised patients taken medicines for current patients 	<ul style="list-style-type: none"> ● Working at the TB section in the HC ● Experience in distributing and watching patients taking medicines

6.3.2 Questionnaires for the qualitative study

The development of the topic guide for the interviews was informed by the pilot study and by issues raised in other qualitative research papers on the subject of adherence to TB treatment in other countries (Munro S, Lewin. S et al. 2007). The first such issue was the distance between the patient's home and the HCs or DOT watcher's home, including travelling time and availability of patient's transportation. The second issue was the relationship between patients and treatment providers such as health staff or DOT watcher, as many studies reported that a patient's relationship with DOT watchers was the factor that could influence patients' adherence to treatment; for example poor follow-up by treatment providers (Nair.D, George.A et al. 1997; Watkins RE and Plant 2004) or carelessness of DOT watchers (Jaiswal A 2003; Greene 2004). The third issue was the issue of choosing treatment providers. The fourth issue was level of understanding of TB treatment among patients and DOT watchers. The last issue was support or the lack of support for patients during the treatment. These issues could all influence patients' adherence to treatment.

The questionnaires were also designed to gather information about how HC-DOT and CDOT are working in Cambodia, which has a cure rate above the WHO target of 85%, and to find out the interaction between patients and treatment supervisors including health staff, and to obtain patients' honest answers about satisfaction with their TB treatment.

6.3.3 Context for the qualitative interviews

The information sought by the qualitative study is outlined in the guide for in-depth interviews for staff (Appendix 10), for patients (Appendix 11) and for DOT watchers (Appendix 12) was:

- Information about the interviewee – eg. sex, age, occupation, where they lived.
- HC-DOT implementation including the arrangement and interaction between patient and staff
 - CDOT implementation including the arrangement and interaction between patient and DOT watcher, patient and staff,
 - Strengths and weaknesses of CDOT and HC-DOT, and
 - Perceptions of CDOT –eg. the views of implementing CDOT among staff at HC, DOT watchers and patients, and how patients feel about receiving treatment with someone other than staff at the HC.

6.4 Data collection methods

6.4.1 Interviews

A. Formal interviews

All interviews were undertaken by the author, and carried out as agreed by the interviewee in terms of convenience of time and place. Most health staff preferred to be interviewed at the HC after 11.00 am in the morning because they were very busy in the early morning. Twenty four health staff were interviewed in the HC, and the other three staff at their home. Sixteen staff from HCs with CDOT were interviewed in this study, and the other eleven from the HC-DOT.

After identifying DOT watchers and patients from the quantitative list, the author asked health staff, village chief or health volunteer for addresses and directions to the DOT watcher's and patient's home. A phone call was used when applicable to arrange the meeting time. From the experience of the pilot study, the author tried to avoid the

research team being brought to the patient's home by staff from the HC, because patients might then think that the research team was from the public sector. This would be likely to affect patients' answers in the interviews.

Most patients and DOT watchers involved in the interviews were from rural areas, so interviews were conducted at their homes or in rice fields. Often, in rural areas interviews conducted at homes attracted the interest of more than one person. In particular family members and neighbors seemed interested and would sit with the interviewee during the interviews. However, we asked them to leave, and tried to find quiet private places for the interviews. Family members were sometimes called to assist when interviewees required. A total of 51 patients (28 CDOT patients and 23 HC-DOT patients) and 18 DOT watchers were interviewed in the study.

Participants interviewed received a sarong (Cambodian traditional skirt) from the author at the end of the interview for their contribution of time to this study. All interviews were conducted in Khmer language with no language barriers. Interviews were tape-recorded with verbal permission from the participants.

B. Informal discussions and feedback

Five interviews and discussions were held with patients' relatives including wives and daughters of patients receiving treatment at home where their treatment supervisors were their family members.

Many issues were discussed with family members, and health staff at the HCs and ODs level throughout the entire data collection period, especially the practical issues for the

implementation of DOT and CDOT approaches and what people in the community think about these approaches.

6.4.2 Observations

Observations on the interactions between new patients treated in 2009 and health staff, and between patients and DOT watcher were also made. However, these observations were only made for patients who were currently being treated for TB in 2009. Four interactions between patients and health staff were observed at the HC while another two interactions between patients and DOT watchers were observed at DOT watchers' homes.

6.5 Ethical issues

Informed consent was agreed and consent forms signed before the interview (Appendix 13).

6.5.1 Autonomy

The participant could refuse to participate at any point before or during the interview. Moreover, participants had the right to not answer any questions which they were not happy answering. In this study, only one participant refused to finish the interview due to her health problems.

6.5.2 Confidentially

All information received from the interviews was kept confidential. The interviews were carried out by the author and one assistant who was a note taker. To ensure confidentiality, the note taker was also asked to keep the information confidential. Only the author could have access to tape records and transcripts.

6.5.3 Anonymity

To maintain the anonymity for participants involved in the interviews, no reference is made to the actual name of participants or to other circumstances that might identify the participants in the results.

6.6 Analysis

All interviews were taped and transcribed. The interviews lasted between one to one and a half hours. After interviews finished, the author was responsible for performing the transcription of interviews in Khmer language and then later translated them into English. Each transcription took between 5 to 6 hours to complete. Data analysis for this qualitative study was done in several steps using thematic content analysis (Daly J, Kellehear A et al. 1997). The thematic analysis method was selected to use in this study because it is a useful method to search for themes that emerge as being important to the description of the phenomenon (Daly J, Kellehear A et al. 1997).

The qualitative data analysis package NVivo 8 (NVivo 2008) was used for the initial stage of coding the themes, which allowed the author to indicate segments of the transcripts and make notes on particular themes. It also allowed complex searching and the ability to link research notes to coding. However, the NVivo package was only used to organise the themes and coding, but not for the data interpretation.

6.6.1 Finding general themes

The first step was to identify general themes regarding the structure of HC-DOT and CDOT, experiences of TB supervision and treatment for both approaches, and perception of TB care towards health staff, DOT watchers and patients. General themes for the

structure of HC-DOT and CDOT included the number of TB staff in the HC, availability of TB tests in the HC, DOT treatment requirement, allocation of patients for treatment, especially place and DOT watcher for patients.

6.6.2 Identifying emergent categories

The second step was to identify the categories of effects of CDOT and HC-DOT approach. This was particularly important in identifying the various factors that could influence patients' adherence to treatment for both treatment approaches.

6.7 Limitation of the data collection for qualitative method

Most patients selected in this study lived in rural areas where the infrastructure is very poor. In some areas the author and research team took more than two hours by car and walking from the HC to get to the patient's home. Finding patients and DOT watchers' homes was not easy as there are no house numbers and the road instructions given by DOT watchers, health villagers or staff at HC were often not very clear. The author tried to arrange meeting times with patients by phone, but not all patients had access to the telephone.

There were several other problems affecting the data collection; the first was migration; some patients were not at home during the author's visit since they worked in the city or had moved to another province. The second problem was not finding the patient's home. The last problem was that a few selected patients had passed away due to other diseases. When these problems occurred, the author interviewed the next patient on the list; this was time consuming, so sometimes the author needed to select patients based on recommendations from health volunteers or local villagers, to identify patients whose

houses were easy to find or who lived close to the main road. This selection may have impacted on the study findings, as patients who lived closer to the main road or the HC, may have less difficulty travelling either to HC or a DOT watcher's house; in particular they may have easier access to DOT information, TB education and treatment than those who lived farther or were more isolated from others in the community. In contrast to patients whose houses were easier to find, those not interviewed because the author could not get access to their houses, may have more negative experiences and face more problems during the treatment, including problems of transportation, difficulty in coming to the HC, the problem of follow-up by staff or DOT watchers, and the level of understanding of DOT and TB treatment may have differed. Furthermore; patients selected in the interviews based on the recommendation by staff or DOT watchers, may have better relationships and more successful treatment compared to those not selected. This may have influenced the findings on interaction between staff/DOT watchers and patients. It is not clear how this may have affected the results, but it is likely that "hard to reach" patients were more likely to benefit from CDOT rather than HC-DOT, as they would have greater transport problems, so to this degree, the benefits of CDOT may be under-reported



Picture 9: Road from the health centre to patient's house



Picture 10: List of community health workers in the health centre

7 CHAPTER 7: Qualitative results for the general arrangement for implementation of DOT treatment in Cambodia

This chapter presents the results of DOT administration in both HCs in Cambodia. Results were based on analysis of the interviews, and where relevant, input from other sources such as observation and notes from informal discussion.

7.1 Characteristic of participants

7.1.1 HC staff

A total of 27 health staff (24 men and 3 women) were interviewed in the study. The ages ranged from 25 to 56 years old. Most of them were primary and secondary nurses; their positions were as directors of HC and persons responsible for TB units including consultation, TB health education, TB treatment or other activities related to TB disease. The majority of health staff participating in the interviews had been working at the HC for more than 10 years.

7.1.2 Patients

Twenty three patients from the 17 HCs treated with HC-DOT, and twenty eight patients from 26 HCs treated with CDOT, were interviewed. Twenty nine patients were women and the rest were men. The ages ranged from 22 to 68 years, and most of them were married. Almost all patients had either no education or had only completed primary school. Most were self employed such as farmers, motor bicycle repairers and

housewives; five patients were primary school teachers. All patients lived in the rural areas and their incomes were less than 2000 Riel (\$0.50) per day. The ethnicity of all patients was Khmer.

Among patients interviewed in the study, 19 had finished their treatment within the last three months, and 14 others had completed the treatment between 3 to 6 months before the interview. Another 5 patients had not yet completed the treatment at the time of interviews; and the remaining patients had finished the treatment more than 6 months ago.

7.1.3 DOT watchers

A total of 18 DOT watchers were interviewed, twelve men and six women, aged from 29 to 68 years. Most DOT watchers had completed primary or secondary school; and they could read and write Khmer. The majority were farmers and some were community health volunteers. All had worked as DOT watchers for more than two years.

7.2 DOT administration

7.2.1 Staff in TB unit

Generally two or three staff worked in the TB unit in each HC. They are responsible for finding suspect cases in the community, TB health education, taking sputum samples and sending them to the laboratory, and watching patients swallow medicines at the HC. Their responsibilities were not only for TB but also for general consultation, PEV program, HIV/AIDS and maternity and child care.

7.2.2 Identifying suspect cases

The first place where patients seek treatment is at the HCs and referral hospitals. Most patients were confident about the government health services, but a few patients went to private clinics, pharmacies or drug stores to buy medicines because of the waiting time in HCs, and would be referred back to HCs by private doctors or pharmacists for further TB tests if TB was suspected. One patient stated:

“First I went to the private clinic near the market. Doctor gave me an injection for 2 days...I still coughed. Then doctor told me to go for the chest X-ray at the hospital.” (HC-DOT patient, male 51 years old)

Some TB cases were found during general consultations and medical check-ups at the HC. As mentioned by most staff and patients, only a few TB patients were referred to the HC by health volunteers or staff, and they were usually living in the same village as staff or close to staff's home. Quote: *“I felt very sick and I went to the HC for the consultation.”* (HC-DOT patient, female 52 years old)

Others involved in referring patients with TB symptoms included neighbors, relatives and friends. As this quote illustrates: *“Because I had similar symptoms as my neighbor who just finished the TB treatment, then he told me to go for TB tests at the HC.”* (CDOT patient, female 59 years old)

7.2.3 TB tests

The most common TB test used was the sputum test. Patients were asked to give three saliva samples over two days. Lung X-rays were not available at the HC level, but only in the main referral hospitals in the city or in some private clinics. Some patients were

referred for X-ray if the sputum tests were negative depending on the distance between the HCs and the referral hospitals and the staff's level of experience.

One staff member noted: *"We have only the sputum tests for TB in our HC. Chest X-ray is available only in the referral hospital which is far from here.... Based on my experience, patients who were smear negative but were very sick and had the TB symptoms; started taking TB medicines right away. A chest X-ray would delay treatment."* (Staff at HC- CDOT, male 40 years old)

All sputum samples need to be sent to laboratories at referral hospitals because the HCs do not have their own laboratories, microscopes and specialists. Sending samples to the laboratory could not be done every day, depending on the location of HC and the distance between HCs and the hospitals. Most HCs are located far from hospitals, some more than 14 kilometers, which would take more than half an hour by motorbike. On average, samples are sent every 3 days if HC is close to the laboratory, but once a week or every two weeks if the HC is very far and transportation difficult.

Quote: *"I take the samples from patients and send them to the laboratory at the referral hospital which is far from here since the HC doesn't have any microscopes and materials. I send them once a week by my motorbike, every time it takes me about 20 minutes to get to the hospital."* (Staff at HC-CDOT, male 41 years old)

Every HC receives \$24 three monthly from the CENAT to send the tests to the laboratory. This covers weekly transport costs. Some staff reported that if the samples needed to be sent more than once a week, they had to pay from their own money. As one staff member noted: *"The \$24 given by the CENAT allows us to send samples 4 times a month. If there are a lot of suspect cases and we need to send the samples twice a week, then our staff*

pay from their own pocket for the transportation." (Staff at HC-CDOT, male 38 years old)

Results were picked up by staff within 1 or 2 weeks from when they sent the new samples. Most patients reported that they were asked to come back to the HC for treatment about 10 days after the sputum samples were taken. Others mentioned almost 15 days before starting treatment, especially patients treated at HCs located far from the laboratory. One patient said: *"It was almost 3 weeks for me until I was asked to come back at the HC for treatment because staff told me that my sputum was sent to the laboratory which is far from our district."* (CDOT patient, male 33 years old)

7.2.4 HIV/AIDS test

In some HCs, an HIV/AIDS test was required for TB patients before starting the TB. This test was available only for HCs with NGO funded TB and HIV programmes. Few patients interviewed in the study had this test.

"This HC requires HIV test for patients treated for TB. I know only my HC and two other HCs in this OD use combined HIV test with TB program because it is funded by CHW (local NGO). The other HCs don't require HIV test for TB patients." (Staff at HC-DOT, male 40 years old)

7.2.5 Direct observation treatment (DOT)

DOT was implemented at the HC level in 2002, for the long course treatment of 8 months; 2 months with staff at HC, and for the other 6 months patients took medicines at home without DOT watcher. The short course treatment (6 months) was fully introduced in 2004; some HCs implemented the ambulatory DOT (HC-DOT) where staff are the

DOT watchers. Others implemented CDOT (DOT in community) where the DOT watchers included chiefs of villages, health volunteers, or family members. Some HCs implemented both types of DOT.

TB treatment, including medicines, is free for everyone within the country, although, patients pay around 4000 Riel (US\$1) for the first consultation. *“During the whole treatment, I paid only 4,000 Riel at first before they took my samples, the rest I didn’t pay anything because TB medicines were free.”* (CDOT patient, female 39 years old)

HCs do not treat relapse patients and multi-drugs resistance patients. These are referred to the referral hospitals or the TB hospital in Phnom Penh.

8 CHAPTER 8: Qualitative results for specific implementation of CDOT

This chapter presents the results for the implementation of CDOT program including the structure, the weakness and strengths of CDOT in Cambodia. The acceptability of implementing CDOT program among staff, DOT watchers and CDOT patients are also presented in this chapter.

8.1 The implementation of CDOT program

The implementation of CDOT started between 2005 and 2006. This program was introduced and established by the CENAT in collaboration with other local and international organizations such as USAID, Japan International Cooperation Agency (JICA), Reproductive and Child Health Alliance (RACHA), Cambodian Health Committee (CHC), Partners for Health and Development (PFHAD), and Save Children Australia (SCA). The CDOT program was a part of the health promotion program activities funded by these organizations. Selection of HCs for implementation of CDOT depended on the availability of sponsored funding. *“CDOT is part of health activities supported by the RACHA, but TB and CDOT are not the first priority for them, because they mainly support maternity and child care, and family planning in the HC.”* (Staff at HC-CDOT, male 40 years old)

While the CDOT program started at the end of 2005, its duration varied between HCs depending on the funding available from its sponsors, with most sponsors funding for 1 to 2 years. During the study period, some HCs had already terminated the CDOT program;

other HCs said that the program would finish in the near future due to lack of funding. One staff member reported: *“My HC has implemented the CDOT since the end of 2005. However, by the end of this year, the CDOT will cease in my HC because RACHA is going to pull out the fund from TB and CDOT. I think this organization run out of funds for CDOT project because they have many activities such as family planning, and mother and child care. They have to decide which one is the first priority for them.”* (Staff at HC-CDOT, male 42 years old)

The implementation of CDOT differed from one HC to another, depending on the policy and program of the individual sponsor. For example, some sponsors such as RACHA, JICA, and USAID provided funds directly to HCs to run the CDOT program. Biannual reports of the number of new TB cases and treatment outcomes were submitted to the sponsors and time to time, inspection teams of the sponsors were assigned to follow-up on the registration, the operational activities and on the way of DOT watchers observe patients in the community.

Quote: *“JICA has provided money directly to our HC to implement the CDOT program. They were not involved in the training and the selection of DOT watchers. Twice a year we need to send them the reports of the number of new cases and treatment outcomes for TB activities. Sometimes their inspectors come to check the reports at the HC and they also go to visit patients and DOT watchers in the community to see how the CDOT is practiced.”* (Staff at HC-CDOT, female 36 years old)

Where the CDOT program was sponsored by CHC, PFHAD, and SCA organizations TB staff of the HCs were only involved in the activities of providing training to DOT watchers and follow-up of patients' adherence to treatment. Other activities, such as the

selection of DOT watchers, delivery of medicines to DOT watchers, and the incentives for DOT watchers were organized by the sponsors.

"We were involved only for the TB training and sometimes go to visit patients and DOT watchers in the community. The CHC selected the DOT watchers for the program; especially this organization paid for the transportation for DOT watchers to come at the HC to collect medicines." (Staff at HC-CDOT, male 40 years old)

HCs implementing the CDOT also used some ambulatory DOT. According to staff 20 to 30% of patients were treated with ambulatory DOT.

8.2 Identifying suspect cases under the CDOT areas

Through the media and health education in the community by staff and health volunteers, patients may decide to seek TB consultation at the HC. The majority of suspect cases came for sputum tests by themselves especially those who live close to the HC. Patients who lived far from the HC were referred by DOT watchers, family, friends, or neighbors. For those who lived very far from the HC and had difficulty to come for the sputum check, DOT watchers were asked to bring the containers with patient's sputum back to the HC.

"If patients couldn't come to the HC, we asked DOT watchers in the village to collect their sputum samples and bring them back to us." (Staff at HC-CDOT, male 26 years old)

8.3 The treatment procedures

In the same way as for HC-DOT, patients with results showing the existence of either TB or extra-pulmonary TB were asked to come back to the HC. Contact was made through staff at the HC, chief of the village, the DOT watchers, friends and their neighbors.

Usually, the contact would be made by the same DOT watchers who referred patients for the sputum check at the HC in the first place.

For patients who could come to the HC, staff explained to them about the DOT including treatment duration, side-effect of drugs, time, place and name of the DOT watcher who would be responsible for watching them during the whole treatment, and especially the consequence of non-adherence to treatment. Patients were asked to sign the agreement form between patients and staff or DOT watchers, in which they agreed to take medicines regularly with DOT watchers for the whole period of treatment. For patients who could not come for their results, DOT watchers were asked to meet staff, who explained about the patient's profiles including name and address, patient's results, type of TB, and the medicines that patients needed to take for the initial and continuous phase: *"After patients were selected for me to take care, the doctor at HC phoned me to tell about patient's names, their TB results, their addresses, and medicines that patients needed to take for the initial phase."* (DOT watcher, male 55 years old)

8.4 Allocation of patients for the treatment under HCs which implemented CDOT

Patients were allocated to either the ambulatory DOT or CDOT based on staff's decisions. Most staff said that patients were allocated to treatment with the ambulatory DOT if they lived less than 5 kilometers from the HC, except patients who were very sick, old, had no transportation, or had other reasons that made them unable to come for the treatment at the HC. The CDOT was used for patients who lived further from the HC or were unable to access the HC every day during the treatment. As a patient said: *"I didn't select where I wanted to take medicines; the doctor at the HC advised me to take*

medicines with the DOT watcher in my village because he knew that I don't have any vehicle to go to the HC." (CDOT patient, female 39 years old)

8.5 Places and DOT watchers for patients treated with the HC-DOT

Patients treated with HC-DOT came to take medicines with staff at the HC from Monday to Friday for the initial phase; during the weekend and national holiday patients were allowed to take medicines at home. During the continuous phase, most patients were allowed to take medicines at home without any supervisor; only a few of these patients in the study took medicines with DOT watchers for the continuous phase.

"I went to take medicines with staff at the HC every morning from Monday to Friday for the first 45 days, and the rest of my treatment I took medicines at home by myself."

(Patient, male 69 years old)

The most important period for the TB treatment is the initial phase, when unpleasant side-effects are most likely, so patients are required to have DOT watchers for their adherence to treatment. For the continuous phase (usually the 3rd-6th months) patients tend to become more comfortable with medicines and they understand the treatment process; so they are allowed to take medicines at home if they could not come to the HC. As a staff reported: *"The first importance of TB treatment that we need to have someone to observe patients is the first two months; after that patients know the time of taking medicines and feel comfortable with medicines. Then we allowed them to take medicine at home."* (HC-CDOT staff, female 53 years old).

Most staff said that patients needed to sign a form to agree to take medicines every day at home until the treatment ended. The treatment cards were checked by staff whenever

patients came to refill medicines at the HC. Some staff mentioned that even though they allowed patients to take medicines at home, they still followed up the patients' adherence to treatment by checking the treatment cards and visiting the patients at home.

8.6 Type of DOT watchers for CDOT patients

According to staff, there were two types of DOT watchers: permanent and temporary DOT watchers. However, the author found out that in practice family members were involved as DOT watchers for some CDOT patients.

8.6.1 The permanent DOT watchers

The majority of DOT watchers involved in the CDOT program were permanent DOT watchers. This type of DOT watchers was a village health volunteer or the chief of village. These people were involved in other health activities for HCs including mother and child care program, family planning, malaria, and HIV/AIDS. Generally, there were 1 or 2 permanent DOT watchers in one village; they were selected by the staff and the sponsors of program. As note by a DOT watcher: *"I am a health volunteer in the village. I am involved in many health programs for the HC. Since 2005 I was assigned by staff and RACHA organization to watch TB patients taking medicines in the community."* (DOT watcher, male 68 years old)

The selection of DOT watchers depended on their educational level, their experience related to health activities, and the relationship between them and staff at the HC or the sponsors. The basic requirement to become a DOT watcher is to know how to read and write in the Khmer language, because they need to tick the patient's treatment cards for the follow-up patient's adherence to treatment.

DOT watchers received 2 to 3 days training with staff at the HC and/or staff from the sponsors before beginning work. The training included TB symptoms, TB educations in the community, definition of DOT treatment, the side-effect of medicines, how to follow-up patients, the consequence of non-adherence to treatment, and how to deal with any problem that can happen during the treatment. However, DOT watchers mentioned that in the trainings TB was just one of many health activities including family planning, maternity and child care, HIV/AIDS, and malaria. One DOT watcher said: *"I have received the training for TB treatment, TB symptoms and how to follow-up patients' adherence to treatment. But the TB training was just one session and the rest of the training was about family planning, malaria, vaccination and HIV/AIDS."* (DOT watcher, male 52 years old)

DOT watchers were asked to come back for a meeting at the HC every 2 or 3 months to review the TB training and to discuss any problems that they faced during their work. However, most DOT watchers said that the regular training happened only a few times at the beginning of the program; up to now they have been asked to come back for the training at the HC only once or twice a year because of the limitation of funds. *"The regular meeting for TB with staff and the NGOs happened only for the first 6 months, due to lack of funds from the sponsor the meeting was reduced to twice a year"* (DOT watcher, female 46 years old)

In addition, the family members of DOT watchers such as spouses and children were also involved in giving and watching patients take medicines when DOT watchers were busy or traveled during the treatment: *"Sometimes when he needed to attend the meetings in*

the city, he asked his wife to bring me the medicines to take at my home before she went to the market." (CDOT patient, male 63 years old)

DOT watchers involved in the study have worked in the CDOT program for more than 2 years. Some DOT watchers have more experience because they have observed many patients, while others have observed only 2 to 3 patients. Most DOT watchers revealed that they could observe 3 to 4 patients at the same time; the number of patients for each DOT watcher was assigned by staff at the HC.

8.6.2 The temporary DOT watchers

Temporary DOT watchers were patient's neighbors, friends or sometimes staff at the HC. They were asked to be involved as DOT watchers from time to time when the permanent DOT watchers were not available in the areas where patients lived. One patient said that: *"Because the health volunteer's house in this village is very far from my house, so I took medicines with Mrs....(name) who lives next door. She is just a housewife."* (CDOT patient, female 38 years old).

Temporary DOT watchers were also used for the continuous phase for ambulatory DOT patients who could not come to the HC and especially for those who did not have any family member living in the same household.

Some HC staff were also involved in giving medicines in the community, especially to those who lived close to staff's house and have difficulty to come to the HC. *"I took medicines with Dr..(name) who lives around 10 minutes from here and also works at the HC."* (CDOT patient, female 67 years old)

TB training sessions were also offered to temporary DOT watchers before they started their work. However, the training was only one day. *“The training that they have received from our staff, it was just basic for the treatment. They were asked to join the training session only half day.”* (Staff at HC-CDOT, male 41 years old)

8.6.3 Family members involved as DOT watchers

Most staff mentioned that employment of family members as DOT watchers for the initial phase was avoided in some HCs because it was not recommended by the NTP in the national guidelines, as it would be very difficult to control the patients' adherence to treatment. *“In this HC, we don't use family members as DOT watchers because patients may not be afraid of their own family members; especially family members using as DOT watchers isn't recommended in the guidelines.”* (Staff at HC-CDOT, male 40 years old)

The involvement of family members as DOT watchers was applied only for the continuous phase of ambulatory DOT patients and some special cases, for example for patients who were very sick, unable to travel, and those who lived far from the HC and health volunteers' house. As stated by one patient: *“Doctor asked my wife to watch and remind me at home for the time of taking medicines every day for the whole 6 months because I was very sick and couldn't go anywhere.”* (CDOT patient, male 33 years old)

Family members who watched patients taking medicines were asked to meet with staff at the HC for briefing about the treatment procedures, patient's medicines, the time to take medicines, how to tick the treatment card, some side-effect of medicines, and the consequence of patient's non-adherence to treatment.

Family members as DOT watchers for the CDOT patients were allowed by most HCs. Many CDOT patients mentioned that family members played a role as DOT watchers by giving and watching them take medicines when their DOT watchers were absent: *“When my DOT watcher was busy, he gave medicines to my son for few days and asked him to observe me until my DOT watcher came back to the village.”* (CDOT patient, female 67 years old).

Even when family member were not assigned directly as DOT watchers they were involved in assisting and encouraging patients to complete the treatment. Family members were involved in reminding patients to take medicines, accompanying patients to DOT watcher’s houses, and going to collect medicines from the HC: *“My daughter encouraged me to continue taking medicines whenever I wanted to give-up due to side effect of drugs. She bought good fruits and desserts for me to take after I took medicines. Sometimes when I was very tired, she helped me to bring medicines from DOT watcher’s house and asked me to take them at home.”* (CDOT patient, female 56 years old)

8.7 The selection of DOT watchers for CDOT patients

The DOT watcher for individual patient was selected by staff at the HC. It was also mentioned that sometimes DOT watchers and patients did not know each other before. One DOT watcher said that: *“I couldn’t select patients; they were assigned by staff at the HC; sometimes I didn’t know these patients before.”* (DOT watcher, male 59 years old)

Some staff mentioned that patients could change their DOT watchers if they were not satisfied with the selection. However, patients did not change their DOT watchers, even though they were not satisfied because they thought that if they changed the DOT

watchers, it could lead to trouble in the relationship between staff and patients during the treatment. *“My DOT watcher was appointed by the doctor; I didn't know him before. We rarely talked every time I went to his house, we didn't have a good communication during the treatment. But I was afraid of asking the doctor to change because I didn't want to have any trouble either with the doctor or the DOT watcher.”* (CDOT patient, male 30 years old)

When asking patients how satisfied they were with the selection of DOT watchers by staff, most said that they were happy because they have known each other before the treatment started. Especially, their DOT watchers were also the village health volunteers, so they could talk directly with them when they have any side-effects: *“I was very happy because he is also a health volunteer. He was like an uncle to me because my father and him are very good friend.”* (CDOT patient, female 21 years old)

8.8 The role of DOT watchers for the CDOT program

DOT watchers played an important role as educators and observers for the CDOT program. They were responsible for finding and referring suspect cases to HCs for TB tests. Their most important job was to give and observe patients taking medicines regularly for the whole 6 months. DOT watchers needed to mark the treatment cards every time the patients took medicines. DOT watchers were requested to report every problem they faced during their work to staff at the HC. Some DOT watchers were responsible for collecting patient's medicines from HCs. As noted by one DOT watcher: *“I need to give medicines and watch patients taking it every morning until the treatment finished. I am also responsible for follow-up patients and encourage them to come taking medicines with me regularly.”* (DOT watcher, male 39 years old). Additionally, some

DOT watchers were also responsible for collecting the sputum samples from patients and bringing them to the HC for the tests.

8.9 The role of HC staff in the implementation of CDOT

Staff at the HC were responsible for providing TB training including training in the guidelines for DOT treatment to DOT watchers at the beginning of their work; staff also needed to review and follow-up the activities of DOT watchers. Even though staff could not see the CDOT patients taking medicines every day, they were responsible for follow-up of patients' adherence to treatment, by going to visit DOT watchers and patients at home; and especially going to check the treatment cards for both patients and DOT watchers. Moreover, staff were also responsible for helping patients whenever they had any problems, such as side-effect of medicines during the treatment.

In some HCs, staff were responsible for transporting medicines to DOT watchers in the community: *"Medicines were brought to me by staff at the HC twice a month."* (DOT watcher, female 46 years old). Moreover, staff were in charge of providing TB education and DOT treatment to people in the community; in particular they were also responsible for finding suspect cases and referring them for the TB tests at the HC.

8.10 The role of NGOs in the CDOT program

As mentioned above all the implementation of CDOT was funded by local or international NGOs. Most NGOs such as RACHA, USAID and JICA provided funds for health promotion which included the TB and DOT training. These NGOs provided funds directly to the TB staff at the HC in order to get more involved with staff for the CDOT program. For example, these NGOs provided the financial support including salary and

transportation fees to staff at the HC for the monitoring and follow-up both DOT watchers and patients: *“RACHA supports our 2 TB staff at this HC with US\$16 per month for training and monitoring the CDOT program and US\$4 per month for transporting medicines to DOT watcher’s house in the community.”* (Staff at HC-CDOT, male 40 years old)

Some NGOs including WRC and SCA put more effort into DOT watchers for the operation of CDOT program by giving rewards to DOT watchers and money for the petrol to collect medicines from the HC: *“The NGO paid me US\$2 per patient who finished the treatment with me.”* (DOT watcher, female 23 years old).

A few NGOs such as CHC were directly involved in follow-up of the patients’ adherence to treatment, and sent their staff to visit patients and DOT watchers in the community to see whether patients have taken medicines regularly with DOT watchers: *“Sometimes CHC sent their staff to check the treatment cards for CDOT patients and to see if patients really go to take medicines with DOT watchers.”* (Staff at HC-CDOT, male 42 years old)

8.11 Places of taking medicines for CDOT patient

The place and time of taking medicines for CDOT patients depended on the agreement between DOT watchers and patients. Most staff said that the CDOT guideline required patients to take medicines at DOT watcher’s house; however, they were flexible and patients could also take medicines with DOT watchers at home or other places that were convenient for both of them: *“We told patients to go and take medicines at DOT watcher’s houses, but they could take medicines any places that were convenient for both of patients and DOT watchers.”* (Staff at HC-CDOT, male 39 years old)

Some DOT watchers brought medicines to patient's house every morning in the case of those who were very sick or unable to travel far from their houses: *"My DOT watcher brought medicines for me to take at home every morning for the first month since I was very sick. But the rest of treatment I went to take medicines at his house."* (CDOT patient, female 56 years old)

It was noted that not all CDOT patients lived close to the DOT watchers. Some patients lived more than 3 kilometers from the DOT watcher's house. Many patients revealed that the distance from their house to the DOT watcher's house and the HC was the same: *"My DOT watcher's house wasn't close to my house. It took me around 15 minutes by motorbike to get to his house. I think it was the same distance from my house to the HC."* (CDOT patient, female 23 years old)

8.12 The duration of taking medicines with DOT watchers for the CDOT patients

Most CDOT patients had treatment with DOT watchers for the initial and continuous phase. A few took medicines with DOT watchers only in the initial phase, while for the continuous phase they took medicines at home by themselves. There were other patients who lived far from the DOT watcher's house, especially those who were very sick, for whom DOT watchers would bring medicines to their home and watch them taking it every day until their sputum control became negative at the end of second month: *"I took medicines with the DOT watcher for only 2 months and the rest I took it by myself at home because my DOT watcher's house is far from here and I had difficulty to walk since I lost one leg."* (CDOT patient, male 69 years old).

8.13 Methods of the delivery of medicines to DOT watchers

The transporting of medicines from HCs to DOT watchers in the community varied from one HC to another depending on the policy of the sponsor. Some sponsors paid HC staff to deliver medicines to DOT watchers while others paid transportation fees directly to DOT watchers to collect medicines from HCs: *"I was paid by the NGOs for going to collect medicines from the HC once a week; I received US\$7 per month."* (DOT watcher, female 23 years old).

Medicines were kept by DOT watchers rather than patients. Generally, medicines were delivered weekly for the initial phase and twice a month for the continuous phase depending on the availability of medicines in the HC. Most DOT watchers said that the delivery of medicines by staff was always on time, but sometimes DOT watchers needed to remind staff at the HC if medicines were nearly finished.

At some HCs, patients collected medicines from the HCs by themselves, or paid DOT watcher to collect medicines for them. One patient said: *"Sometimes I and my wife were busy and we couldn't go to collect medicines at the HC. I paid the petrol for my DOT watcher about 6,000 to 8,000 Riels."* (CDOT patient, male 33 years old)

8.14 Follow-up the patients' adherence to treatment for the CDOT patients

CDOT patients were required to have 3 treatment cards; one card for staff at the HC and the other two for the DOT watcher and patient. Patients and DOT watchers needed to tick the date on the cards every time patients have taken medicines. Both treatment cards were verified by staff. Most staff and DOT watchers mentioned that staff went to check the treatment cards once a week or every time they brought medicines to DOT watchers.

During the visit by staff, medicines were checked and compared with the date on the cards to see if patients have taken medicines regularly: *"Staff came to my house once or twice a week during the continuous phase to check the patient's yellow card and count the medicines, to see whether I gave medicines to patients correctly or not."* (DOT watcher, male 59 years old)

Some staff visited patients at home were dealt with based on whenever they passed by patient's house to check treatment cards and the patient's health status and to see if patients have any problem including side-effect of medicines. Visits by staff depended on the location of patient's houses, the patient's profile and the health status of each patient as reported by DOT watchers, and would be made more often for patients who often missed the treatment sessions with DOT watchers or who had very serious side-effects: *"During my treatment, staff came to see me at home only 2 to 3 times because I didn't have any side-effect of drugs. But during the time of my father's treatment, he had very serious side-effects; staff came to see him at home every 3 to 5 days for the first month."* (CDOT patient, male 25 years old)

Both DOT watchers and patients mentioned that the patients' homes were visited by DOT watchers the same day if patients did not show up for the treatment sessions in the morning. In the absence of DOT watchers, medicines were given to patients by DOT watchers' family members. Most DOT watchers said that medicines were prepared by them before being given to their family members. They taught the family members how to observe and tick the date on the treatment cards. When asking them what made DOT watchers believe that their family members did not make any mistakes related with dosage and the number of medicines, most replied that their family members have already

seen their activities in giving medicines to patients every morning, so they should not make any mistake. Patients also know the number and color of medicines since they took them every day: *"I left medicines for patients with my wife when I was busy because I already taught her about medicines; especially the packages of medicines for the individual patient were prepared by me. She has never made any mistake because she saw me giving medicines to patients every morning."* (DOT watcher, male 59 years old)

The DOT watcher was the first person patients sought for help whenever they had any problems including the side-effect of medicines. Most DOT watchers mentioned that minor side-effects were dealt with them based on their own experiences; severe side-effects of drugs would be reported to staff at the HC, and sometimes patients needed to go to see staff at the HC: *"I had very bad side effects of drugs in the first week. I told my DOT watcher and she told me that it was just the reaction of medicines; she asked me to drink the coconut juice after I took medicines. She also asked me to take some vitamins; it helped."* (CDOT patient, female 21 years old)

Most staff mentioned the government strategy to motivate and follow-up patients' adherence to treatment, namely the gifts that patients receive during the treatment. The gifts included 60 kg of rice, salt, dried fish and vegetable oils for TB patients treated with DOT. These were provided by the government and the World Food Organization (WFO), and given to patients twice during the 6 months treatment when patients completed the first 3 months and at the end of treatment. They were both an incentive and an aid to recovery. Patients, who missed or interrupted treatment, were excluded from the gift list: *"Another reason to make patients complete the treatment is the gifts that patients receive from the government. It would motivate patients to finish the treatment. If they don't take*

medicines regularly or give up the treatment, they wouldn't receive these gifts." (Staff at HC-CDOT, male 41 years old)

8.15 The attitude of DOT watchers to CDOT patients

The hospitality of DOT watchers and their family members was mentioned by most patients. Most patients said that their DOT watchers never discriminated against them and they provided full supports including time and encouragement to patients during treatment. For example: *"My DOT watcher and his family have never discriminated me because of my disease. He devoted his time for me and he encouraged me to finish the treatment. Sometimes he waited for me when I was late, he never got angry; and sometimes he went to visit me at home when I didn't go to his house in the morning."* (CDOT patient, male 30 years old)

When asked if they worried about the disease being transmitted by patients to their family members, most DOT watchers mentioned that they did worry, and requested patients bring their own water to take medicines; they also asked patients to wear face masks and cover the mouth with a scarf when patients approached their residences: *"I asked patients to wear face masks and cover their mouth when they came to my house; especially when talking to me or to my family."* (DOT watcher, male 52 years old).

8.16 The experience of TB stigmatisation and discrimination by CDOT patients

Many studies patients mention the stigma associated with TB. This stigma has existed in Cambodian culture for many years; however, nowadays through the media and TB health education, the public have a better understanding about the cause and transmission of disease, and so the problem of TB stigmatisation in the community has significantly

decreased. Many patients in this study said that people in the community including their neighbors and friends never discriminated against them for being treated with TB: *"I think that people have better understanding of this disease, so I and my family members didn't have any experience of TB stigmatisation during my treatment. My villagers including my neighbors have known my disease but they never discriminated against me and my family. In contrast, they even tried to encourage me to finish my medicines once they saw me having side-effects of drug."* (CDOT patient, male 51 years old). Moreover, most patients said that they shared their experience of treatment with friends and people in the community in order to increase awareness of TB among people in the community.

However stigma was experienced indirectly by a few patients who felt that although other villagers understood about TB they still decided to isolate themselves in order to avoid the risk of TB transmission: *"My friends and neighbours did not discriminate against me but I did not want to transmit this disease to them...Every time I went to the rice field, I could eat with them and I knew that they wouldn't say anything.... But I decided to take my meal alone, because I was not sure whether they were afraid of my disease or not."* (CDOT patient, male 30 years old). Others experienced stigma from their CDOT watchers. As mentioned above most patients were requested by CDOT watchers to bring their own water to take medicines, and were asked to wear face masks and cover their mouths with scarves when approaching the DOT watchers' houses. Whether this reaction should be classified as stigma or not is difficult to say. It could also be interpreted as a normal reaction to a serious and contagious disease, and the effect of this decreased stigmatisation in Cambodia is undoubtedly to increase the willingness to access diagnosis and treatment and thus limit the spread of the disease.

8.17 Incentives for the involvement of DOT watchers in the CDOT program

Most DOT watchers received small incentives for their involvement in the CDOT program. The incentives for DOT watchers differed from one HC to another, again depending on the sponsors. Some DOT watchers received only material support such as T-shirt, clothes, bags, and bicycles, while others received money for their involvement in the training sessions: *"Since I started my job, I have received only one bicycle in the beginning of my work, it was 2 years ago and now the bicycle is broken."* (DOT watcher, male 59 years old).

Although DOT watchers received some money, the amount was very small and couldn't support their costs: *"I was paid by the NGOs US\$2 per patient but this amount wasn't sufficient for the transportations fees that I have paid for the petrol to go to collect medicines from the HC."* (DOT watcher, female 23 years old)

DOT watchers also received support in kind from the government. Consultation fees and the fees for delivery of baby at the HC or the referral hospital were free for DOT watchers and their family members: *"Because of my work as a DOT watcher, I and my family don't need to pay for the consultation fees at the HC."* (DOT watcher, male 29 years old)

Some DOT watchers received small gifts from patients such as fruits, vegetables, and meat; they rarely received money from patients: *"Some patients when they felt better, they gave me some fruits or foods for their thanks."* (DOT watcher, female 56 years old). Similarly, one patient said: *"My DOT watcher has never asked me for any money, but sometimes I gave him small gifts such as chicken or pork. It was just my gratitude."* (CDOT patient, male 22 years old)

8.18 “No-DOT” patients

Some patients in HCs where the CDOT was implemented took medicines at home without any supervisor for the whole treatment. Staff let patients take medicines at home without any supervisor for four reasons. The first reason is if patients were well educated and understood TB disease, such as the head of village, staff believed they were committed and able to complete the treatment: *“I took medicines at home by myself. I didn’t need anyone to observe me because I used to be a health volunteer in this village as well; I already knew the treatment procedure.”* (Patient registered as CDOT patient, male 43 years old)

The second reason is the patient’s job; patients who did not have a permanent job in the village where they lived but travelled for work were allowed to take medicines at home or their work places, and needed to come to the HC at least once a month to meet staff and collect medicines: *“In the past, I used to allow several patients taking medicines at home without any DOT watcher because of their carrier background. Those patients likely worked as constructors; they came back to their home town when they were sick. It was very difficult for us to follow-up them due to their works; they moved around more often from one village to another.”* (Staff at HC-CDOT, male 42 years old).

The third reason is the patient’s health status and the availability of DOT watchers in the village where patients lived. Patients who were very sick and had difficulty in coming to the HC and a DOT watcher was not available in the areas where patients lived, would be allowed to take medicines at home: *“I took medicines at home, no DOT watcher...I was allowed by the doctor because I didn’t have any vehicle and the DOT watcher in this*

village lived far from my house." (Patient registered as CDOT patient, female 62 years old).

The last reason is to do with the relationship between patients and staff at the HC. Staff allowed patients taking medicines at home when they knew each other well: *"Doctor at the HC and my uncle are good friends. So he let me take medicines at home instead of going to the HC."* (Patient registered as CDOT patient, male 28 years old)

Of the patients registered as CDOT patients and selected for interview in the study, most were "non-DOT" patients because they took medicines by themselves at home. The most usual reasons for this were lack of transportation, no availability of DOT watchers and the patient's health conditions.

"Non-DOT" patients were followed up by staff at the HC; most staff mentioned that the patient's home visits were made 3 to 4 time during the treatment, more for patients who had very serious side-effects and for those who lived close to staff's house: *"When I started medicines for the first 2 weeks, the doctor from the HC came to visit me more often because I had very bad side-effects."* (Patient registered as CDOT patient, male 55 years old)

"Non-DOT" patients were asked to come to the HC for medicines four times per month for the initial phase and twice a month for the continuous phase. Family members of patients could also collect medicines at the HC.

The involvement of family members in reminding patients to take medicines at home and encouraging patients to finish the treatment were mentioned by all “non-DOT” patients. One patient said: *“When I took medicines at home, my son always reminded me every morning before he went out to the rice field.”* (Patient registered as CDOT patient, male 66 years old)

8.19 Sputum controls for CDOT patients

The TB treatment guideline requires that the first sputum controls for smear positive patients be done at the end of the initial phase. Medicines for the continuous phase would be given to patients if the results were negative, otherwise patients needed to stay on the intensive phase medicines for one more month. The second controls are at the end of the fifth month before the treatment is finished.

Patients with DOT watchers in the community were asked by staff at the HC or DOT watchers to come for sputum control. Staff would remind DOT watchers in advance to tell patients when needed. A few staff contacted patients directly: *“A week before patient needed to have the sputum control; I reminded DOT watchers to tell patients on what date sputum needed to be taken to the HC.”* (Staff at HC-CDOT, male 26 years old).

Patients could also send their sputum samples to the HC through DOT watchers or family members. Containers for the sputum samples were left with the DOT watcher.

However, many patients disclosed that they had no sputum control during the treatment, while a few patients only had one at the end of the initial phase. According to patients, sputum controls were rarely done for two reasons; the first reason was that patients were

not informed about the time for the sputum tests by staff or DOT watchers. Because most patients rarely visited the HC, patients could find out about the time for the sputum controls only through their DOT watchers: *"I didn't have any sputum controls during my treatment because the doctor and my DOT watcher didn't tell me when I needed to recheck my sputum."* (Patient registered as CDOT patient, male 55 years old)

The second reason was the patients did not have sputum after they took medicines for a few months, because the mucus had disappeared: *"I didn't have any sputum control because I felt better and no more mucus to take."* (CDOT patient, female 62 years old)

However, some patients who did not have the sputum control complained that they still had TB symptoms. Those patients were not sure if they were really cured of TB; some patients even asked for more medicines during the interviews: *"I am not sure whether the TB in my body was completely cured because I feel weaker than before and I couldn't work hard as before. Sometimes I coughed with blood. I also reported to doctor at the HC last month; he told me that my TB was cured but it is just the trace of the TB in my lung. But I don't think so, maybe I should take more medicines."* (Patient registered as CDOT patient, male 55 years old)

When the author asked staff what made them think that the patients were cured, since some of them did not have any sputum control, most said that they believed that if patients took medicines regularly for 6 months, TB would be cured because that is what it said in the DOT treatment guideline. Others mentioned that patients could have the symptoms such as cough or tiredness but it was just a trace of the TB that could appear sometimes when patients worked hard. *"After the 6 months treatment, patients are*

already cured but some signs could appear when patients work hard in the rice field.”

(Staff at HC-CDOT, male 41 years old)

8.20 TB education and promotion in the areas where the CDOT was implemented

TB education, including finding suspect cases and TB treatment itself, was done by staff and DOT watchers. Staff went into the community once a month to educate people about health activities including TB. For the HCs that have received support from the NGOs for the implementation of CDOT, staff have opportunity to go to the community more often to educate people compared to the ordinary HCs. Moreover, DOT watchers involved in the CDOT program also provided TB education, DOT information and case finding (finding new suspect case among the villagers). Most DOT watchers mentioned that they were often having meetings with the villagers to provide information about TB education and treatment; they particularly tried to find people with TB symptoms and encouraged them to go for TB tests at the HC.

8.21 Advantages of the implementation of CDOT program

There are several advantages that were raised by staff, DOT watchers and patients based on their experience of the CDOT program.

A. Staff's qualification

Some staff felt that one of the successes of the implementation of CDOT was the capability of staff in providing sufficient TB training and education to DOT watchers. Most staff mentioned that they have a lot of experience in TB training from both government and NGOs, so they could provide this TB knowledge to DOT watchers and guide them in its implementation in the community: *“Even though we don't watch*

patients taking medicines every day, we have trained our DOT watchers based on our experience, how to give and observe patients, especially we guide them when they have problems." (Staff at HC-CDOT, male 40 years old)

B. DOT watchers motivation

The involvement of DOT watchers in the whole CDOT program, by referring new cases and giving and watching patients take medicines everyday in the villages, was felt to be the key success of CDOT. Most staff opined that even though the incentives for DOT watchers were very small, they were still involved in observing patients take medicines regularly and sometimes coming to collect medicines at the HC: *"The good point is that the DOT watchers in our HC are very active. They have received only small incentives from the program but they still want to be involved in this job. They help us by referring suspect cases and observe patients taking medicines."*(Staff at HC-CDOT, male 40 years old).

Patients liked the DOT watcher's attitudes. Most patients were happy with their DOT watchers, because they were treated with respect and provided with emotional support to finish the treatment. Some DOT watchers and their family members also provided food or money to poor patients: *"My DOT watcher was very nice and helpful, he never discriminated me and my family. He tried to help me by asking if I have any problems or side-effects. In the first month when I started my medication, he encouraged me to finish my medicines every time I met him."* (CDOT patient, male 22 years old).

Other patients mentioned that they appreciated the time DOT watchers devoted to patients during the treatment. Patients revealed that the waiting time for taking medicines with

DOT watchers at home was not an issue because DOT watchers were there when patients arrived. *"I liked to take medicines with my DOT watchers because she has never let me wait for her; every time I arrived at her house, she was there and waiting for me."* (CDOT patient, male 58 years old)

Another key factor that encouraged patients to take medicines with DOT watchers was the relationship between patients and DOT watchers. Some staff mentioned that some patients felt more comfortable in discussing any issue related to health problems (as well as other issues) with their DOT watchers than with staff at the HC. Patients felt they could talk openly and freely with DOT watchers since they may have known each other and may even live in the same village: *"Some patients hardly shared anything with our staff because they were afraid of us. However, they were very happy to take medicines with DOT watchers in the community because they could share all problems and other issues including everyday life with their DOT watchers. I felt that some patients were more comfortable to take medicines with DOT watchers than our staff."* (Staff at HC-CDOT, male 26 years old).

C. The implementation of CDOT is convenient for patients

Most patients mentioned that taking medicines with DOT watchers in the community was less stressful because they were not required to wake up so early in the morning, and a convenient and flexible time schedule could be negotiated between patients and DOT watchers. Moreover, patients said that CDOT allowed them to engage with normal daily activities during the treatment: *"I was very happy to take medicines with DOT watchers because I didn't need to go the DOT watcher's house early in the morning since his house*

is close to my house. I could send my kids to school first before going to take medicines with him." (CDOT patient, male 33 years old).

D. The CDOT program saved patients' expenditures

All patients, DOT watchers and staff agreed that the main advantage of CDOT was the reduction of cost and time to patients, as the costs of travelling were reduced: *"I think that taking medicines in the community saved my costs for the transportation."* (CDOT patient, female 39 years old).

CDOT also saved patients from long waiting times for treatment at the HC, allowing more time to engage with other aspects of their lives: *"I like to take medicines in the community because I didn't need to wait for the arrival of staff at the HC. Every morning I spent only 10 to 15 minutes to take medicines with DOT watcher, after that I could go to work as usual."* (CDOT patient, male 46 years old).

E. CDOT increased the patients' adherence to treatment

The implementation of CDOT increased patients' adherence to treatment because the time and place were convenient for patients, so they could take medicines regularly without any interruption: *"Because it was convenient for me to take medicines at DOT watcher's house located close to my house, I went to take medicines every day..... If staff asked me to take medicines at the HC, I would give up because I don't have any vehicle."* (CDOT patient, female 39 years old)

When asking patients how they felt taking medicines with DOT watchers who were not medical professionals, most patients stated that they trusted them because they have

known each other for long time; especially since most DOT watchers were village health volunteers, so they were the first person patients would go to seek for help whenever they had any health problems. *"I was happy to take medicines with uncle DOT watcher because I have known him since I was young and he was liked my uncle."* (CDOT patient, male 22 years old).

F. CDOT increased the TB awareness in the community

Another advantage of the CDOT was increased awareness of TB among people in the community; which could reduce the chain of TB transmission among villagers: *"Now my neighbor had coughed for 2 weeks, I told her to go for the sputum check at the HC. I told her that the treatment is effective like she saw me taking medicines with the health volunteer and now I feel better."* (CDOT patient, female 56 years old)

The implementation of CDOT also helped to reduce TB stigmatization in the community by letting people understand that TB is an infectious disease that can be cured by taking medicines regularly for 6 months. One patient stated: *"Taking medicines in the community could let people understand more about TB. The villagers knew that I had TB.....but they didn't discriminate me and my family because they have understood that TB isn't an heredity disease."* (CDOT patient, male 30 years old).

G. CDOT is better than self-administration treatment

Some patients said that taking medicines with DOT watchers was better than taking medicines at home without any supervision. Without the DOT watcher patients may not take medicines regularly because they could forget the time or they could stop taking medicines when they felt better. This could increase the risk of default and multi-drug

resistance in the future: *"I think taking medicines with DOT watchers is better than taking medicines at home alone because we may forget to take."* (CDOT patient, male 25 years old)

8.22 Disadvantages of CDOT program

A. Lack of follow-up of CDOT patients by staff

However HC staff visiting CDOT patients in the community could be problematic, firstly due to time constraints. *"Most patients go to take medicines with DOT watchers very early in the morning, like 6 o'clock. So I couldn't go to see every patient because I need to send my kids to school and my wife to the market."* (Staff at HC-CDOT, male 54 years old).

A further reason is the lack of money to allow follow-up of patients in the community; staff needed to pay for petrol from their own pockets if they went more often to see patients in the community: *"We couldn't go to see every patient treated in the community because the amount of money that we receive for transportation couldn't cover the petrol to see every patient, as some patients live very far. Sometimes I need to pay for the petrol from my own pocket if I go to see patients three times per month."* (Staff at HC-CDOT, male 42 years old)

It was also mentioned by patients that the visit by staff during the treatment was not enough especially during the first two months when most patients have very bad side-effects. *"During the treatment staff came to see me only 4 times, 2 times for the initial phase and another 2 times for the continuous phase. I wanted him to come to visit me*

more often during the initial phase because I had very serious side-effect of medicines."

(CDOT patient, female 34 years old)

B. DOT watcher's qualification

Many HC staff were concerned about the lack of knowledge among DOT watchers because they were not medical professionals. *"Honestly, I don't really trust DOT watchers observing patients because I couldn't see the interaction between DOT watchers and patients every day. Sometimes I went to check the treatment card and I saw days on the treatment card were missing but DOT watchers responded that they forgot to tick but medicines were given to patients."* (Staff at HC-CDOT, female 36 years old)

Some staff were also concerned that DOT watchers may not supervise strictly in the long term. They may allow patients to take medicines at their home without supervision, so it could lead to many problems such as non-adherence to treatment, drug overdose and MDRs in the future: *"We are worried that DOT watchers may allow patients taking medicines at home; they couldn't watch patients taking medicines regularly. If this problem happened more often, it could be increased the number of defaulters and MDRs."* (Staff at HC-CDOT, male 26 years old).

This problem was also mentioned by many patients- DOT watchers allowed them to take medicines at home whenever patients requested, especially when DOT watchers were busy: *"When I went to pagoda for few days, my DOT watcher allowed me to bring medicines. Sometimes I took medicines at my home too because my DOT watcher was busy."* (CDOT patient, female 67 years old)

Further problems were mentioned by staff, for example that some patients missed medicines for a few days because of the absence of DOT watchers, or medicines ran out during the treatment but DOT watchers did not inform staff at the HC: *"No matter how much effort we put to DOT watchers they aren't disciplined in their jobs. As happened in the past, some patients missed medicines for 1 to 2 days because DOT watchers weren't at home. Sometimes DOT watchers didn't inform us when medicines finished."* (Staff at HC-CDOT, male 40 years old)

Staff also mentioned that too low or an overdose of medicines could be given by DOT watchers. This was more likely to be done by DOT watchers who have received traditional medical background such as traditional healers; they may change the patient's medicines without any discussion with staff at the HC because they think they have full knowledge of the medication. For example, some DOT watchers decided to reduce the number of pills for patients without any discussion or permission from staff when patients have side-effects of medicines: *"In the past, 2 patients took medicines with me and they had very serious side-effect of drugs. I decided to reduce her pills from 8 to 4 tablets per day, and I gave her some medicines for her fever. Then, I started to give her back 8 tablets per day when she felt better."* (DOT watcher, male 68 years old)

C. Lack of incentives for DOT watchers

DOT watchers involved in the CDOT program were not paid for this job, so they could not devote their time only for TB patients and TB activities. One DOT watcher said: *"The weak point of CDOT is the lack of rewards and incentives for DOT watchers. I don't earn anything from this job, sometimes I need to pay my own money for the petrol whenever I go to visit patients at home."* (DOT watcher, male 44 years old).

Moreover, some DOT watchers resigned from the CDOT program: *"Since 6 months ago, I resigned from the DOT watcher because I am very busy with other work. Especially I didn't get any pay roll or salary from this job."* (DOT watcher, male 59 years old)

D. Insufficient DOT watchers for CDOT program

An inadequate number of health volunteers involved as DOT watchers for the CDOT program was reported by staff and patients. Normally, there were 2 or 3 health volunteers in one community; but one or two of them were selected to be DOT watchers because the program provided only small benefits. As mentioned by staff that sometimes DOT watchers needed to supervise 3 or 4 patients at the same time, so patients may select self-administration as the treatment method: *"I took medicines at home by myself because DOT watcher wasn't available in my village. My village used to have one DOT watcher but he passed away and the HC hasn't yet appointed new DOT watcher."* (Patient registered as CDOT patient, male 55 years old)

E. The environment of patients treated with the CDOT

Some staff believed that taking medicines with DOT watchers was not as strict as the HC because DOT watchers were not medical staff; in fact, sometimes they were good friends, so patients may not really listen to their advice. A similar issue was also raised by DOT watchers, that some patients didn't listen to their advice and did not have the commitment to come for taking medicines. Some DOT watchers mentioned the irregularity of the patient's visits to the DOT watcher's house; some patients did not arrive on time while others did not show up: *"In fact, it is difficult for me to deal with some patients who didn't listen to what I said, for example I told them what time they should come to take*

medicines with me. Sometimes, I needed to wait for them because they arrived late or they didn't show up for the treatment sessions." (DOT watcher, male 59 years old)

Another complaint about the CDOT program was that some patients received insufficient information, and some patients felt that DOT watchers did not provide enough information regarding TB medicines, when and how long to take the medicines, and the date for the sputum controls: *"I didn't know why I needed to take a lot of pills for the first 2 months because my DOT watcher never told me."* (CDOT patient, female 38 years old)

F. Lack of opportunity for selection of DOT watchers

Some patients complained that they did not have a choice in selecting their DOT watchers because DOT watchers were selected by staff. A few patients were not happy because their DOT watcher's houses were further than the HC. *"My DOT watcher's house was further than the HC. It was the same road to the HC but it was nearly 1 more kilometer farther down from the HC. I didn't know why staff wanted me to take medicines with her."* (CDOT patient, female 21 years old)

G. Delay in getting the sputum controls for CDOT patients

Some staff revealed difficulty in getting sputum samples from some CDOT patients at the end of second and fifth month, and they were not sure about techniques that DOT watchers used to collect samples and transport them to the HC because DOT watchers were not really health professionals.

H. Too few TB staff in the HC

Patients taking medicines with DOT watchers in the community still required staff at the HC to follow-up and check their adherence to treatment, but the numbers of TB staff at the HC was not enough. Because of this, the follow-up of patients in the community was reduced.

8.23 Perceptions of the implementation of CDOT among staff

When asking staff at the HC what they think about the implementation of CDOT based on their experiences, some were not really supportive of the CDOT program because they were concerned about the quality and effectiveness of CDOT. Staff recommended that the ambulatory DOT approach should be used for the initial phase for every patient who could come to the HC, because staff could see and follow-up patients taking medicines every day. However, CDOT could be applied during the continuous phase when the sputum controls become negative; also CDOT could be applied to some patients who are seriously sick or have difficulty to come to the HC every day: *"I think every patient who could come to the HC; should come to take medicines with us for the first 2 months and the rest 4 months they could take medicines with DOT watchers in the community. However, DOT watchers could also ask to observe those patients who have difficulty to access the HC."* (Staff at HC-CDOT, male 42 years old).

Staff were agreed that CDOT could reduce cost to patients and family but it could increase patients' non-adherence to treatment if follow-up by staff and DOT watchers failed. Some staff were concerned that DOT watchers would not be supervised as strictly as staff at the HC and some patients may stop taking medicines when they felt better. Staff felt that taking medicines with staff at the HC is stricter than with DOT watchers

because patients are afraid of staff. One staff opined: *"I am not sure if DOT watchers supervise patients as strict as our staff. I am afraid that the number of non-adherence to treatment for CDOT patients may be increased if DOT watchers failed to follow-up patients because patients may stop their treatment when they get better."* (Staff at HC-CDOT, male 54 years old)

As mentioned by staff, CDOT would be applied if the program had enough funds for both DOT watchers and staff. It could be done by providing more incentives and more benefits to DOT watchers, so it would allow them to devote their time to encouraging and watching patients complete the treatment. Moreover, the implementation of CDOT could not be done without supervision from staff at the HC; most staff suggested that providing enough money for transportation to staff at the HC would allow them to regularly visit patients and DOT watchers in the community: *"I think if we really want to fully implemented CDOT, we need enough funds for DOT watchers and our staff. DOT watchers should receive more benefits that would allow them to work hard and strictly supervise patients. Especially, our staff should have enough funds for the transportation that would allow us to follow-up patients in the community more often."* (Staff at HC-CDOT, female 36 years old)

8.24 Perceptions of the implementation of CDOT among DOT watchers in the community

Most CDOT watchers strongly supported the CDOT program because they felt that the implementation of CDOT could provide a lot of benefits to patients especially for those who were very poor. They thought that patients treated in the community could save a lot of time and money on the transportation. It was also useful for patients who were very

sick and lacked transportation. Moreover, CDOT allowed patients to engage with their normal daily activities because the waiting time for taking medicines with DOT watchers was not a problem: *“I think that patients taking medicines in the community are happy because they don’t need to go to the HC every day, patients could save money on the travelling expenses. It is also more convenient for those who are very sick and don’t have any vehicles.”* (DOT watcher, female 56 years old).

When asking CDOT watchers how they felt about giving medicines and observing patients take them every day for the whole treatment; most responded that they were very happy to do these jobs because they felt that they could help to reduce the workload to staff at the HC, and more especially they could help people in the community to become free from TB: *“I am very happy to watch patients taking medicines in the village because I could help staff at the HC, especially I could help my villagers. I want everyone in this village to get free from TB.”* (DOT watcher, male 55 years old)

However, some suggestions were made by many CDOT watchers about ways to improve the implementation of CDOT; the first is to increase of incentives for DOT watchers. CDOT watchers suggested that the program should give them more incentives such as a salary for DOT watchers and funds to cover the costs for going to visit patients at home or collect medicines from the HC: *“I would like to suggest that our DOT watchers should receive more benefits, for example salary for DOT watchers....It would make us to motivate in this job because we want to help but we also need money to support our family as well.”* (DOT watcher, male 59 years old)

Another suggestion was to increase the number of visits by staff to DOT watchers and patients in the community. Most DOT watchers proposed that staff from the HC should make more frequent visits to DOT watchers and patients at home, especially for the initial phase since most patients had very bad side-effects from the drugs. *"I would like to suggest that staff should come to visit and follow-up patients in the community more often. I could only observe patients taking medicines but I don't know what to help patients for the side-effects of drugs."* (DOT watcher, male 44 years old)

The last recommendation by CDOT watchers was to receive more training and feedback from staff; most said that the training sessions which they received were not enough or were out- dated. Others mentioned that they would like to receive feedback from staff and NGOs regarding their work and TB treatment in the community.

8.25 Perceptions of the implementation of CDOT among patients

CDOT patients' opinion of taking medicines in the community varied. Most patients agreed that CDOT was flexible and saved transportation costs, and allowed them to engage in their normal activity. Moreover, CDOT was very convenient for those who were seriously sick and had difficulty in travelling to the HC. Some patients mentioned that they got a lot of encouragement and support from their DOT watchers during the treatment; this motivated them to take the medicines regularly: *"Thanks to my DOT watcher who always gave me the encouragement to finish my medicines. I wanted to stop the treatment because the side-effects, but he tried to encourage me and he also gave me some medicines to reduce it."* (CDOT patient, male 30 years old)

However, many CDOT patients felt that follow-up by staff from the HC was not sufficient; especially TB education and the DOT information that they received through DOT watchers was not adequate compared to those treated at the HC: *"I felt that my DOT watcher didn't have enough experience for TB treatment because every time I asked him about medicines and side-effect of drugs he didn't answer me immediately as he needed to ask staff at the HC."* (CDOT patient, female 48 years old). All CDOT patients requested more regular visits by staff during the treatment.

Some patients said that CDOT would be better if staff allowed them to select their own DOT watchers. Even though CDOT patients were nearly always happy with the selection of their DOT watchers by staff, they still felt that staff should discuss with them first before making decision. Patients felt that as the TB treatment required patients taking medicines for 6 to 8 months, so patients preferred to take medicines with someone who has a good relationship with patients: *"I think that if I need to treat for TB again, I would like to select my own DOT watcher because I didn't have any choice to select my own DOT watcher. I think it is importance to take medicines with someone who you are well known because the TB treatment is very long."* (CDOT patient, female 38 years old)

When asking patients who they would prefer to take medicines with during the treatment; the answer was mainly family members, because taking medicines with family members was convenient for most patients, since they did not then need to travel to another place. Patients revealed that although patients took medicines with DOT watchers during the treatment, family members were still involved in encouraging and motivating patients to come and take medicines every day. *"If I could select my own DOT watcher, I would choose my wife because she was very good in reminding me for time to take medicines."*

Especially, it would be more convenient for me to take medicines with her at home."
(CDOT patient, male 58 years old).

There were similar responses from patients with self-administration treatment, they were happy to take medicines at their home rather than travelling to another house. They also mentioned that their family members were involved as DOT watchers as well as in giving medicines, collecting them from the HC, and reminding patients of when to take the medicines: *"I was happy to take medicines at my house because it was convenient for me. When I took medicines at home, my son observed me taking medicines every day."*
(Patient registered as CDOT patient, female 52 years old)

In addition, patients who had the sputum controls before the treatment finished, were very happy about taking medicines in the community because they felt that the treatment was effective. In contrast, those who did not have any sputum checked during the treatment were still questioning their health and the effectiveness of treatment. They felt that the DOT watchers may have given them the wrong doses of medicines because some TB symptoms still persisted. A few patients thought that if they had been treated by staff at the HC from the beginning, they would be cured. One patient opined: *"I felt that I am not completely cured from TB because I still cough blood. I think maybe my DOT watcher didn't give me the right dose for my medicines. Now thinking back, I should have taken medicines with staff at the HC because they could see me and give me the right medicines."* (CDOT patient, female 47 years old)

8.26 Results from the observation

During the data collection, the author found that the real number of patients treated with CDOT in some HCs was less than the figures given in the register. The helping based on the number of CDOT patients, provided by sponsors or NGOs was the reason for the staff to increase the figures of number of CDOT patients in order to get more support. Moreover, there was a lot of self-administration patients among patients registered as CDOT patients.

CDOT patients rarely went back to the HC unless they had very serious side-effects. It was also disclosed by staff that they had never met some patients because they were registered through the DOT watchers. During the data collection, some patients were selected from the register by the author for the interviews; however, these names were not recognized by the villagers when the author visited.

Another problem found by the author was relapse of some CDOT patients and self-administration patients in HCs which had implemented CDOT. Two patients selected in the interviews were relapse patients who had been treated for TB before. Both of them involved self-administration for the first treatment. *"This is my second time for TB treatment. I started my first treatment last year but that time I took medicines at home by myself."* (CDOT patient, female 47 years old)

9 CHAPTER 9: Qualitative results for implementation of HC-DOT

HC-DOT, also known as ambulatory DOT, started in 2002 at most HCs in the study. Most patients treated with HC-DOT live within 5 kilometers of the HC. The most common mode of transport to the HC is walking, by bicycle or by motorbike.

9.1 The treatment procedures

Most sputum positive patients were contacted to come for treatment by phone call, through health volunteers, the chief of village, neighbors or relatives, or HC staff if they lived in the same commune.

The DOT information including treatment duration, side effects of drugs, time, place and person responsible for watching patients, and the consequences of non-adherence to treatment were explained and discussed with patients on the day that treatment started. Interactions between staff and new TB patients were observed during the study, and patients were seen to be advised by staff to come to the HC every day to take medicines for 6 months; and the patients took medicines in front of staff. Side effects of the drugs were explained by staff before giving the medicines.

9.2 Flexibility in place of treatment for HC-DOT patients

Other DOT approaches such as DOT at home and CDOT were also used in the HCs implementing ambulatory DOT, with assignment based on staff's decision. Staff allowed patients to take medicines at home for the whole treatment if they were old, very sick,

disabled or unable to come to the HC every day. Some patients were assigned to CDOT according to the availability of health volunteers in the village. For example: *“I went to take medicines at the HC for 3 days and the rest I took medicines at my home because the staff knew that I had difficult to come to the HC every day since my house is far and I live alone.”* (HC-DOT patient, female 28 years old)

9.3 Places and DOT watchers for patients treated with HC-DOT

Patients could take medicines while observed by any staff member in the HC because the TB medicines for each patient is prepared every morning. In contrast to the national TB guidelines for HC-DOT which requires patients to come for taking medicines at the HC supervised by staff for 6 months (MoH 2004), both staff and patients reported that patients came to take medicines at the HC only from Monday to Friday for the first two months for the initial phase, and for the other 4 months they were allowed by staff to take medicines at home. Furthermore, in the intensive phase patients were allowed to take medicines at home during the weekend and national holidays: *“Patients are required to take medicines with us at the HC only for 2 months at the beginning and the rest they could take at home. During the treatment with us at the HC, we give them medicines to take at home during the weekend and holidays because nobody is here.”* (Staff at HC-DOT, male 41 years old).

Some patients took medicines with staff at the HC for the continuous phase, especially those who lived close to the HC. For patients taking medicines at home, they were required to come back to the HC once or twice a month to restock with medicines.

Most patients admitted that they rarely went back to the HC during the continuous stage, since their family members or friends helped them by collecting the medicines. Others mentioned that they went back to the HC either because staff asked them to go back or because they had other health problems, otherwise they took medicines at home for the remaining 4 months. One patient said: *“After 2 months, I took medicines at my house; my son helped me collect medicines from the HC every Monday. Since then I never went back to the HC.”* (HC-DOT patient, female 57 years old)

There was generally no DOT watcher to observe these HC-DOT patients taking medicines at home during the continuous phase. Almost all the patients and staff mentioned that, as patients become accustomed to taking medicines on a regular basis at the HC for 2 months and as their desire to be cured grew, there was no need for anyone to monitor them taking medicines at home for the rest of the treatment: *“At home no one watched me taking medicines, I took medicines every morning before going to the rice field. I didn’t need anyone to watch me; I knew when I needed to take it. I’ve never forgotten to take medicines because I wanted to be cured and get back to my regular works.”* (HC-DOT patient, male 48 years old).

Although patients did not have anyone to observe them during the treatment at home, family members such as a spouse or children were involved in reminding patients of the time to take medicines. One patient said: *“At home my wife reminded me to take medicines before I went to work.”* (HC-DOT patient, male 51 years old)

9.4 The CDOT used for HC-DOT patients

CDOT was used in some HC-DOT for patients who had difficulty coming to HCs. Health volunteers and the chief of village were used as DOT watchers. These health volunteers did not receive any payment from the TB and DOT program as patients were not officially CDOT patients; they were paid from other program funds, such as the family planning program, or the malaria, mother and child care, and vaccination programs.

Staff were responsible for selecting health volunteers as DOT watchers for patients depending on the distance between the patients and the DOT watchers' homes, especially the availability of health volunteers in the village where patients lived. One staff member stated: *"For patients who live far from the HC, I need to check if there is any health volunteer available in their villages. If there is, I will send patients to take medicines with the health volunteers in the village instead of coming to HC."* (HC-DOT staff, female 42 years old)

Patients treated with the CDOT revealed that they took medicines at a DOT watcher's house everyday including the weekend and national holidays. Those responsible for watching patients taking medicines were not only health volunteers; but included their family members whenever health volunteers were busy. However, patients were still required to come to the HC once or twice a month to collect their medicines and leave them with health volunteers: *"Doctor asked me to take medicines with Mr....who is involved in the health activities in the HC. He lives close to my house. I went to take medicines with him every morning including Saturday and Sunday."* (Patient, male 55 years old)

9.5 Non- DOT patients

Most patients who had treatment at home for the whole 6 months did not have any DOT watcher observing them taking medicines, although a few patients were observed by their family members.

There are several situations where staff allowed patients to take medicines at home. First, if patients refused to have treatment if they were not allowed to take it at home, due to difficulty to travel to the HCs, and there was no availability of health volunteers in the village where patient came from. Second, during the period of flooding, patients were allowed by staff to take medicines at home because it was very difficult to access HCs. *“To tell you the truth, we still let patients take medicines at home. We asked their family members to observe patients at home. We don't have any choice...since our HC is located far from the villages where patients live. Some patients come from villages more than 5 km from this HC. Especially, last year our HC was flooded for over 5 months and we let patients take medicines at home instead of coming to the HC.”* (HC-DOT staff, male 41 years old)

Of HC-DOT patients interviewed in the study, almost half were “non-DOT”, because they had no supervisor, neither staff nor health volunteers at home, for the whole 6 months. Reasons for not being observed daily by staff at the HC were distance from patient's house to the HC, the difficulty of transport and the patient's health conditions: *“Because my body hurts and my home is very far from the HC, I had no strength to walk. I asked the doctor to take medicines at home instead of taking with her at the HC.”* (HC-DOT patient, female 40 years old)

Many of these patients still went back to the HC weekly to collect medicines for the initial phase, and once a month for the continuous phase. Others said that they went back to see staff at the HC more often during the initial phase, in order to seek help for side effects. Most patients treated at home mentioned that their family members helped and reminded them to take medicines at home.

9.6 Follow-up of patients' adherence to treatment for HC-DOT patients

Follow-up of patients' adherence to treatment was by checking the patient's treatment cards. Most patients mentioned they were told to tick the day in the treatment card every time they took medicines at the HC or at home. Those who took medicine at home needed to bring the card for staff to verify whenever they came for collecting medicines at the HC. Medicines were not given if any days of taking medicines were missing from the treatment card, and patients would be asked to come back to have treatment with staff at HC. One patient said: *"To avoid forgetting taking medicines at home, I was told by doctor to tick in my treatment card every time I took medicines. I needed to bring the card to show him whenever I went to see him."* (HC-DOT patient, male 49 years old)

When asked what made staff believe that patients were really taking medicines regularly at home, most answered that they believed in the patients' desire to be cured and to avoid transmitting TB into the family. Several staff members commented that the family members were asked to observe and remind patients taking medicines at home. Staff also checked with the patient's family to see and make sure if patients really took medicines regularly at home: *"I investigated closely with patients. I believe that they must take medicines everyday because every patient wanted to be cured, so that's why they came to seek the treatment with us."* (HC-DOT staff, male 56 years old)

If patients missed treatment for at least 2 days they were contacted by staff to come back to the HC, with the contact made through health volunteers, neighbors, and the chief of the village. Several staff stated that they went to visit at home those who missed treatment more than twice. However, most staff said that non-adherence rarely occurred; it only happened sometimes with patients who migrated to other places and those who died during the treatment.

9.7 Sputum controls for patients treated with HC-DOT

As with CDOT patients, smear positive patients were required to have sputum control twice during the treatment. In fact, these controls were rarely carried out due to two factors; the first was the difficulty in sending samples to the laboratory and delays in receiving back the results. Many staff at HCs revealed that the sputum controls were not necessary since the laboratory's staff considered sputum samples for current patients as their first priority. That is why staff rarely asked patients for sputum controls unless they found patients still had some TB symptoms. *"Delays in receiving the results for sputum controls was always happening in my HC. Staff at the laboratory don't consider the sputum controls as the first priority since they had a lot of samples for new patients to check before they could do the controls. Then I decided to give medicines to patients for the continuous phase without waiting for the results since I knew the smears must be negative after patients took medicines for 2 months. However, I still asked for smear controls from those who still had some TB symptoms."* (HC-staff, male 36 years old)

The second factor was that patients did not have any sputum because mucus had disappeared after patients took medicines regularly more than 2 months. The same reasons were given by most patients, that they did not have any sputum control during the

treatment. *"I didn't have any control. My sputum tests were checked only at the beginning. I didn't know that we needed to have the controls since staff didn't ask for it."* (HC-DOT patient, male 49 years old).

When asked what made them think that they were cured since they did not have any sputum control most patients mentioned that they felt better and all TB symptoms had disappeared after the treatment finished: *"I really feel better. I don't have any more blood when I cough. I start to work as normal. Before the treatment I could not work and I felt tired all the time. Look at my health condition now."* (HC-DOT patient, male 51 years old). Others reported that they were told by staff at the beginning of treatment, that they would be cured when they took medicines every day for 6 months.

However, some patients, especially patients who took medicines at home and had no DOT watcher, questioned the effectiveness of TB medicines, because some TB symptoms remained. Some patients asked the author if they could continue to take more TB medicines; others said that they felt hopeless because their symptoms became more serious: *"I still cough with blood, my health doesn't get better since my treatment finished. I don't want to go back for the treatment again since I am very old and I am going to die one day."* (HC-DOT patient, female 55 years old).

9.8 TB education and promotion in the areas covered by HC-DOT

As for CDOT, TB education and health promotion activities in the villages, were done by staff at the HC and health volunteers, although due to lack of funding, they were rarely done from the TB education program, but combined with others health promotion,

whenever they go to see people in the villages, and they ask health volunteers to help find suspect cases in the community and refer patients with TB symptoms to the HC.

Patients said they hardly saw staff from the HC come to do TB education in the villages. Rather they heard about TB symptoms and the DOT treatment through media such as TV and radio. *"I haven't seen staff at the HC come to talk about TB in my village. I heard about TB and the treatment through radio."* (HC-DOT patient, male 51 years old)

9.9 Advantages of HC-DOT

A. Staff motivation

When asked about the key success of implementation of HC-DOT, answers differed. Most patients said that motivation and encouragement from staff at the HC caused them to complete the treatment. One patient expressed the idea: *"I continued to take medicines even though I had very bad side effects because of my doctor. He tried to explain to me and encourage me to take medicines everyday when I saw him at the HC."* (HC-DOT patient, male 43 years old). Most patients mentioned that they were really happy and liked the treatment with HC-DOT because staff were very friendly and never discriminated against patients. A few liked the way staff were very flexible with patients who were very sick or lived far away from the HC by letting them take medicines at home.

Staff also saw encouragement as an important aspect of treatment. Most staff stated that they tried to find suspect cases in the community and to see patients at home if they missed treatment, even though they had to spend their own money for transportation: *"I think one advantage of HC-DOT is the staff's encouragement to patients for taking*

medicines every day; we always tell and remind them about the advantages of taking medicines every day.” (HC-DOT staff, male 56 years old)

When “non- DOT patients” were asked what made them continue to take medicines regularly even though they have not been observed by anyone at home, most said that it was the encouragement of staff at HC to motivate and encourage them to take medicines every day. The effective TB treatment process and explanations by staff before started the treatment including the consequences of missing taking medicines, was a big influence. *“I never forgot to take medicines; I came to take medicines at HC every day. If I had a trip far away from my house I always requested medicines to take during my trip because I knew from staff that if we didn’t take medicines regularly, then my disease wouldn’t be cured.”* (HC-DOT patient, female 28 years old)

Staff’s attitudes including their emotional support and help to reduce side effects of medicines; were key factors in helping patients stay in treatment until the end, even when they had serious side effects and were tempted to interrupt the treatment: *“I had very bad side effects after I took medicines for 3 days. I wanted to stop taking medicines. But the doctor told me those problems would go away, and he gave me some medicines to help for those side effects. I felt better after that. I am thankful to him. If I didn’t treat with him, I would give up from the beginning.”* (HC-DOT patient, female 40 years old)

B. Staff’s qualification

As with the CDOT program the staff’s qualification and experience was one of the advantages of the successful implementation of HC-DOT. Some patients felt more secure taking medicines with staff at the HC because they have a lot of experiences in TB field,

and are the best if something wrong appears during the treatment: *"I felt safer when I took medicines with the doctor at the HC because he could watch me and intervene anytime when I had something wrong including side effects."* (HC-DOT patient, male 33 years old)

C. The environment in HCs

Some patients believed that the stricter environment of the HC was more likely to ensure their adherence to complete the treatment: *"Because I feared having a bad record at the HC for my family. I needed to come back and take medicines every day in the presence of the doctor."* (HC-DOT patient, male 40 years old)

Others mentioned that it was an advantage that the patients got clinical care beside TB, health education and encouragement and support from other patients: *"Every day when I came to the HC, I met with doctors who give me and my family advice and supervise about general health education. I met with other patients who came to take medicines as well; this would encourage me to do the same."* (HC-DOT patient, female 30 years old)

D. TB medicines

Medicines being available and delivered on time from the top levels to the HC, were reported as a key factor in implementing HC-DOT by most staff and patients. *"I like to treat with the HC-DOT because every time I come to take medicines, doctor always had medicines for me."* (HC-DOT patient, male 51 years old)

All patients were very happy with the treatment because of the effectiveness of the medicines, even though side effects were complained of by most patients.

E. Involvement from the health volunteers in community

According to staff, the effective implementation of HC-DOT needs the involvement and effort from people in the community such as health volunteers and chiefs of the village, as well as family members in searching and referring suspect cases to HCs, and following-up and encouraging patients to complete the treatment. Even though most HCs implementing ambulatory DOT have not officially involved health volunteers as DOT watchers, health volunteers were still very much involved in TB activities including TB education in the community, referring patients and helping patients with transportation to the HC. One patient said: *"I like the treatment at the HC because they have a lot of networks in the village. During my continuous phase, sometimes I didn't need to go to collect my drugs since the doctor sent them through Mr..who works as health volunteer."* (HC-DOT patient, female 52 years old)

F. Ambulatory DOT is better than the hospital DOT

Few patients who had a family history of TB treatment under the hospital DOT, mentioned that treatment with the ambulatory DOT was much better since it did not require them to stay at the hospital during treatment. They still could stay in the family and work as normal people during the treatment: *"I am happy to take medicines with staff at the HC because I could stay with my family. It was better than my father's time. He needed to stay at the hospital for 2 months; it was difficult for us to go to see him in the hospital."* (HC-DOT patient, male 25 years old)

9.10 Disadvantages of HC-DOT

A. Problem of access to the HC

Patients and staff at the HC recognized that HC-DOT involved longer travel time and greater distance for patients. Therefore, the effort and time needed to attend the treatment at HCs everyday might affect patient's adherence to treatment, especially for those who were very sick and had no transportation. *"I find it was difficult for me to travel to the HC every day during the treatment because I needed to wake up early in the morning and walk from my house to the HC. Sometimes I was very scared of a traffic accident because I needed to cross the main road."* (HC-DOT patient, female 68 years old)

The financial burden of transportation was complained of by most patients who regularly attended the HC in the initial phase. Travelling to the HCs every day cost patients a lot of money, especially those who were poor and lived far away from the HC: *"Going to the HC every day has cost me a lot of money. I live far from the HC, I had only one bicycle. I had to borrow a motorbike or bicycle from my neighbors when my wife took bicycle to the rice field. Sometimes I had to take a motor taxi; it was very costly to my family because we are very poor."* (HC-DOT patient, male 40 years old)

B. Long waiting time at the HC

The inconvenient appointment times and long waiting times for treatment at the HC were also reported by staff and patients. Most staff said that they asked TB patients to come for medicines earlier in the morning before they have to see new patients. Patients have to wait for staff to complete their duties before giving medicines to patients if they come during the busy times: *"I went to the HC every morning; I arrived at the HC around 7 am. Even though I tried to get the HC around that time but I still had to wait for the*

doctor because staff weren't there yet...only cleaner was there, sometime I waited for 20 minutes." (HC-DOT patient, male 49 years old)

C. No option for the alternative DOT

A few patients treated with the HC-DOT complained that staff did not give them a choice to decide where to take medicines. Decisions were made by staff at the HC, and choices were given only to patients who were friends or related to staff: *"I was not happy with doctor's decision; I live very far from the HC but doctor still asked me to come for taking medicines at the HC. During my time, I saw one lady who lived very close to the HC but she could take medicines at home because she is the staff's cousin."* (HC-DOT patient, female 53 years old)

D. Delay in getting the test results

Delaying in getting back the results from the laboratory and starting the treatment were mentioned by most staff and patients. Many patients reported that they tried to find alternative medical treatment such as traditional medicines or cultural Holy Spirit during the period of waiting for results from the HCs. Some patients needed to come back to the HCs several times in order to seek the results; it was very costly for them in transportation and time: *"Because I haven't heard any news from staff at the HC...it was already 2 weeks. My wife asked me to go to the uncle who is a fortune teller to see if something was wrong with me during my work in the forest."* (HC-DOT patient, male 53 years old)

E. Lack of follow-up from HC staff during the continuous phase

Lack of follow-up from staff during the continuous phase was raised by nearly all patients during the interview. Staff were more attentive to patients' problems during the intensive

phase. Most patients mentioned that staff never visited patients at home to see whether patients had any problems such as side effects of the new medicines: *"I felt that staff only cared for patients during the first two months. When I took medicines at home, he never came to see me or asked me whether I still had any side effects."* (HC-DOT patient, female 59 years old)

F. Lack of TB education and TB promotion in the community

Most patients treated with the HC-DOT felt that the TB education in their communities was not sufficient, because they rarely saw staff educate people about TB. Finding suspect cases in the community is not enough, since the HC's network in the community is still weak. For example, there are not enough health volunteers involved in the TB activities including referral of suspect cases to the HC.

9.11 Perceptions of CDOT from people in HC-DOT

Staff and patients had differing perceptions towards CDOT.

A. Advantages of CDOT amongst people in HC-DOT

The majority of staff and patients recognised that treatment with CDOT would save time, be more convenient for patients, and could reduce the financial burden on the patient's transportation. CDOT was seen as a good method for those who have difficulty in coming to HCs during the treatment. One HC-DOT patient treated with CDOT asserted: *"When I took medicines with my health volunteer in the community, it saved me a lot of time; and if I went to the HC every day, I would pay a lot of money on the transportation."* (HC-DOT patient, female 40 years old). Many patients reported that they would recommend CDOT to other patients and their relatives because it saves time and

money. Some staff mentioned that implementation of CDOT would reduce the workload for the HC and improve TB knowledge among people in the community.

B. Disadvantages of CDOT considered by people in HC-DOT

Both patients and staff saw advantages to CDOT, but were concerned about several issues relating to its implementation. The first issue was their lack of confidence in using health volunteers as DOT watchers. Most staff feared to let patients take medicines with health volunteers because they felt they did not have sufficient TB knowledge and training, especially in solving patients' problems including managing side effects. Patients also commented that they would prefer taking medicines with staff at the HC. Health volunteers could not help them if patients had any problems during the treatment since they are not doctors and less experienced in TB training. One patient stated: *"I don't want to take medicines with health volunteers in the community because they are not doctors and I am afraid of giving me the wrong medicines."* (HC-DOT patient, female 53 years old)

The second issue was that staff were worried that health volunteers may not always supervise strictly in the long term, and so would affect patients' adherence to treatment. Others mentioned that observing patients taking medicines every day by health volunteers may not be possible, because they have many jobs including their own job as well as other health activities in the community, and so they may not dedicate their time 100 per cent to DOT. For example, they may not sit and wait at home for patients to come to take medicines.

The last issue was the lack of incentives for health volunteers as DOT watchers. Several staff who had experience in the implementation of CDOT mentioned that the success of CDOT implementation depended on giving incentives to DOT watchers. If DOT watchers get paid then they will do a good job in TB treatment such as watching patients take medicines, following-up patients' adherence to treatment and referring the suspect cases to the HC. However, the implementation of CDOT could create more difficulty for patients and the HC if there was not enough financial support or incentives for DOT watchers. If DOT watchers were not paid, they would not pay attention enough to observing patients. It would then create difficulty for the HC by increasing the number of defaulters and multi-drug resistant patients.

As mentioned by one staff who had a bad experience with CDOT: "Two years ago, we tried to implement CDOT for those who lived far from the HC by asking health volunteers to be DOT watchers. However, we didn't give them any financial support to do this job; only T-shirts and bags. At first they have done a very good job by coming to collect medicines for patients and reported back to the HC if patients had any problems including side effects. But after a while they stopped coming to the HC because we had no more T-shirts and bags. Then patients started to complain about the absence of DOT watchers. When we checked with patients, we found that some medicines were not given them. Since then we have implemented only the ambulatory DOT because we were afraid of letting patients take medicines with DOT watchers in the community - it could cause the multi-drug resistance." (HC-DOT staff, male 42 years old)

Regarding the implementation of CDOT, most staff commented that CDOT should be implemented during the continuous phase, where patients can take medicines at home.

However, during the intensive phase, patients should come to take the medicines with staff at the HC because then staff can see patients' adherence to treatment. Others mentioned that the CDOT would be appropriate for patients who are very sick and have difficulty to come to the HC: *"It is good to implement the ambulatory DOT for the intensive phase so staff could follow-up patients take medicines every day, and the CDOT could implement in the continuous phase when patients take medicines at home."* (HC-DOT staff, male 36 years old)

"Non-DOT patients" mentioned that they were happy to take medicines at their home rather than to go to take them with anyone else, and if there is the requirement from the HC, they said family members are the best DOT watchers since they live in the same house: *"Why I need to go to take medicines with health volunteers. I am happy to take at my house. But if they require me to have DOT watcher, I could ask my son to watch me; he was the one who reminded me taking medicines when I treated with TB last time."* (HC-DOT patient, female 59 years old).

Others said they would not be comfortable taking medicines with anyone beside staff at the HC, as they would feel a lack of privacy taking medicines with health volunteers: *"I don't want treatment with health volunteers because it makes me feel that everyone in the community would know about my disease. I prefer to come for taking medicines with staff at the HC."* (HC-DOT patient, female 36 years old)

9.12 Results from the observation

From the observation during the interviews at the HC, the author found that more "no-DOT" patients existed in the HC-DOT because most patients took medicines at home

without any DOT watcher. Family members especially husbands and children helped patients by collecting medicines at the HC.

During the study the author found that six of twenty three patients were considered as relapse cases, because they still had TB symptoms such as coughing blood, lost weight and difficulty in breathing. All these patients were “no DOT” because they took medicines at home and nobody observed them for the whole treatment.

During the informal meeting in the village, people complained about the lack of TB education and promotion in the community; they asked the author to bring this issue to the center in Phnom Penh. As stated by one family member: *“I have never seen staff come to do TB promotion in our village. My husband didn’t know about his TB symptoms. He was very sick for more than 2 months. I spent a lot of money buying drugs from a pharmacy because I thought it was just a normal flu. I took him to the HC when he coughed blood. If we knew that his symptoms were TB, we would have gone to the HC right away.”* (Patient’s wife 38 years old)

Villagers suggested improving TB education and promotion activities in the community by creating a channel to find suspect cases with symptoms such as cough and referring them to the HC as soon as possible. Moreover, it can reduce the chains of transmission in the community; and this could be done by HC staff coming to educate people in the villages more frequently.

9.13 Summary key findings of CDOT and HC-DOT from the qualitative study

The implementation of CDOT was recognized by staff, DOT watchers and patients as helping patients to reduce costs of travelling to the HC and saving patient's time, which in turn would allow patients to engage in other economic activities. Patients treated by staff at the HC needed to spend more time in the HC for taking medicines compared to CDOT patients; and needed to spend money on the transportation fees for travelling to the HC every day. However, some staff and patients thought that patients who took medicines in the community may not be as strictly supervised as patients at the HC. CDOT patients felt that they received less regular health education compared to those treated at the HC.

Several problems including delays in getting the results from the laboratory, lack of funds for TB education and promotion in the community, lack of follow-up by staff, and lack of funds for staff and DOT watchers were apparent in both HCs with implemented CDOT and implemented ambulatory DOT. Moreover, neither CDOT patients nor ambulatory DOT patients had any choice of the place or person for their treatment. Self-administration patients existed in both HCs and some still had TB symptoms.

The key finding from this part of the study was that there was significant involvement of patients' family members in watching patients take medicines, reminding patients for the time, encouraging patients to complete the treatment, and helping patients to collect medicines from the HC. According to the national DOT treatment guideline, family members were not recommended to select as DOT watchers; however, in practice family members are involved in patient's treatment more than DOT watchers. Most patients in both settings were very pleased with the care they received from their DOT watchers.

10. CHAPTER 10: Discussion and Recommendations

The present study is the first of its kind to assess the existing CDOT program in Cambodia. The thesis examines CDOT compared to HC-DOT in the country in terms of treatment success and TB case notification. More specifically it aims to understand the implementation of CDOT and HC-DOT in the field especially in rural areas where the infrastructures are weak, and identifies gaps and issues related to their implementation based on the experiences of staff, DOT watchers and patients. The findings are important in designing and adopting TB control interventions that are relevant, sensitive and acceptable to the local people. This chapter discusses how the findings contribute to current implementation of the DOT approaches, makes suggestions as to how they could be improved, and finally makes recommendations for future studies

10.1 The effectiveness of CDOT compared to HC-DOT in the systematic review

It was clear from the systematic review that the effectiveness of CDOT in terms of success of treatment was the same or better when compared with HC-DOT. CDOT would therefore maintain roughly the same high treatment success for smear-positive TB as HC-DOT (RR=1.05, CI: 1.01-1.10).

10.2 The effectiveness of CDOT compared to family-DOT in the systematic review

Although family-DOT is not recommended in the national guideline in Cambodia, this approach has been used in different settings including Thailand, Nepal, India, and Tanzania. Based on the systematic review and analysis in this study, I have shown that

the treatment success for smear-positive patients treated by CDOT is better than for family-DOT (OR=1.33, CI: 1.20-1.48).

10.3 The effectiveness of CDOT in Cambodia

In 2005 CDOT was fully implemented in some areas in Cambodia, with the main goals being to maintain treatment success under the DOT program, to improve case finding, to improve the patients' adherence to treatment, and to reduce the travelling costs for patients.

A. Treatment success rate under CDOT

The quantitative study in this thesis showed that the first goal of implementing CDOT in Cambodia has been successfully achieved, in that CDOT has proved to be as effective as HC-DOT in maintaining high treatment success rates of over 85%, in line with WHO targets.

The treatment success rate of all TB forms among patients treated with CDOT was 97.1% and that of HC-DOT was 96.57% (OR=1.26, 95% CI: 0.56-2.82). The death rate from new-smear positive TB was small and decreased in the areas where CDOT was implemented compared to HC-DOT areas (OR=0.33, 95% CI: 0.11-0.99). Moreover, this study showed that in the same CDOT areas, the death rate among all TB patients was reduced significantly after the implementation of CDOT (OR=0.37, 95% CI: 0.15-0.92), and the treatment success rate slightly improved from baseline (2002-2003) to two years (2006-2007) after CDOT was implemented (OR=2.10, 95% CI: 0.95-4.62).

Key Message: the first conclusion of the thesis is that the effectiveness of CDOT in Cambodia confirms the results of the systematic review of this study. The

implementation of CDOT has maintained at least the treatment success rate of HC-DOT.

It is seen from the literature review that the cure rate of smear positive TB in Cambodia has remained high (95% in 2010) compared to the WHO target of 85%. However, the qualitative study found that most patients, for all TB forms in both DOT approaches, did not have sputum control at the end of treatment but, as patients who had completed the treatment informed the author, they were nevertheless registered as “cured patients” in the registration book at both HC and OD levels. This practice could impact the accuracy of data on cure and treatment completion rates within the country. In some cases, the actual cure rate of smear positive TB could be lower than the rate reported.

Key Message: the second conclusion of the thesis is that the lack of sputum control for patients in both CDOT and HC-DOT areas during treatment could bias the estimates of cure and treatment completion rates in Cambodia.

B. TB case-finding under CDOT

TB case finding for smear-positive in the CDOT program areas increased dramatically from 2002 to 2008, although this increase was not significantly greater than for HC areas without CDOT ($p=0.547$). The results from the quantitative study showed that TB case finding for smear-positive in HCs with and without CDOT increased every year from 2002 until 2008; the improvement of TB case finding in both HCs could be the result of two factors. The first factor is the effectiveness of the DOTS strategy which includes a government commitment to sustain TB control activities, diagnosis by quality ensured sputum-smear microscopy, and standardized recording and reporting systems. Since adopting the DOTS strategy, the NTP has tried to put more effort into TB control

activities by decentralizing the DOT program from hospital-based DOT to HC-DOT in every HC from 2002; so TB education and health promotion could more easily be disseminated to people in the community, especially to those who live in rural areas. The second factor is that the health care system, living conditions for people and Cambodian education have improved every year, so people in the community know more about hygiene, TB awareness and where to seek help when they are sick. This could increase the rates of TB case finding and reduce the death rate due to TB.

Based on the results of the qualitative study, there appear to be two reasons why the TB case finding is similar between HCs with and without implemented CDOT; the first reason is insufficient TB education and health promotion in the community. Even though HCs with implemented CDOT are supposed to have more TB activities in the community, such as DOT watchers finding and referring new suspect cases to the HC, this involvement from DOT watchers could not be carried out in every HC because of insufficient funding of the CDOT program from sponsors. Some sponsors gave incentives to DOT watchers to find and refer suspect cases for sputum checks at the HC, so these DOT watchers would be more actively involved in educating and finding new suspect cases in the community. However, in fact most new patients in both HCs came for TB tests at the HC by themselves and were not identified by the DOT watcher; more patients who lived far away and had difficulty in getting to the HC, were referred by DOT watchers or friends. This would indicate that TB education and health promotion in the areas with implemented CDOT is still weak. The involvement of health volunteers in HCs with only ambulatory DOT regarding the TB education and health promotion in the community, and in finding and referring new suspect cases for TB tests, was the same as DOT watchers involved in CDOT areas.

Key Message: the third conclusion of the thesis is that the goal of implementation of CDOT in order to improve TB case finding has not yet successfully reached the target. In Cambodia, TB case finding has improved in both HCs since 2002 when the NTP decentralized the DOT system to the HC level. Even though the CDOT approach has been implemented, the TB education and health promotion program in the community is still weak due to lack of funding.

C. Selection of HCs to implement CDOT

Since CDOT was introduced and piloted in Cambodia, from 2004 until the period of the study in 2008, not every HC within the country has implemented it. It was clear from the quantitative study that the selection of HCs to implement CDOT was based on where treatment success rates were low, and death rates were high, compared to HCs not selected for CDOT. Moreover, the qualitative results show that even though CDOT was introduced by the NTP, the implementation of this program depended heavily on the availability of sponsors or NGOs who could provide funds to support the CDOT; however, most of these sponsors did not put the CDOT program as their first priority as their main goals were focused on other health activities. During the study period, the implementation of CDOT was terminated in some HCs due to lack of funding from the sponsors. This confirmed the NTP report conclusions in 2007 that CDOT was withdrawn from 41 HCs because there were not enough funds from the NGOs (NTP 2007).

Key Message: the fourth conclusion of the thesis is that the implementation of CDOT program in Cambodia has depended on funding from sponsors. The NTP and CENAT have not had funds to implement CDOT in every HC in the country.

10.4 Impact of the shortage of human resources for the implementation of the DOT program

The numbers of TB staff at the HC is insufficient to cover the TB health activities, because staff also have responsibility for other health activities such as the PEV program, maternity and childcare, and general consultation. Generally, of the three or four staff who work at each HC, two or three work in the TB unit. The TB staff are overloaded, which means too little time for staff to go to the community for TB education, finding suspect cases, and follow-up of patients during the treatment period. Studies by Kabongo (Kabongo D and B 2010) and Wandwalo (Wandwalo E 2006) showed that CDOT can help to reduce the workload of health staff and free up more time to allow staff to provide quality services to other patients. In contrast, this study found that HCs which implemented CDOT still carried out the ambulatory DOT. So staff who work at the HC with implemented CDOT had more responsibilities for TB activities than the regular TB staff at the HC-DOT. It might explain why the large majority of patients in HCs with implemented CDOT said that the follow-up of patients in the community during the treatment was limited.

Key Message: the fifth conclusion of the thesis is that the shortage of TB staff at the HC could impact observation of patients' adherence to treatment and TB education in the community. In particular, it would impact the implementation of CDOT, because of shortage of staff time to follow-up patients and DOT watchers in the community.

10.5 Impact of smear test implementation at the HC level

Most patients' treatment was based on the results of a smear test, while other TB tests including chest X-rays were rarely done because of lack of facilities available at the HC.

Few sputum negative patients were referred for X-rays at the referral hospital or private clinics before starting treatment, while others started treatment without any further tests. Decision-making about starting treatment for sputum negative patients was based on staff experience. This process could have advantages and disadvantages; the advantage is that if the staff's decision is correct, patients could start treatment immediately and it would reduce the chain of TB transmission in the community. However, if the patient had another disease, the TB patient could receive inappropriate treatment.

Another issue at the HCs is the delay in sending smear samples and in receiving the results back from the laboratory. This delays treatment and increases the TB transmission in the community; in particular it increases the patient's costs including transportation fees and time. The results from the qualitative study showed that patients needed to travel several times to the HC to receive their diagnosis results.

Lack of sputum control before terminating treatment was clear from the qualitative study; half the patients interviewed in this study had no sputum control before their treatment finished; among these, were some patients who still had TB symptoms and who wanted to restart their treatment.

All staff interviewed mentioned that they wished to have their own laboratory in the HC because that would reduce the time to receive the results of smear tests, and in particular save travelling costs to staff transporting samples and going to pick up the results back from the laboratory, which was often done at their own expense.

Key Message: a sixth conclusion of the thesis is that there is a lack of sputum control and an issue of delay in sending the sputum samples and receiving the results back

from the laboratory in both HCs with and without implemented CDOT. Few patients have sputum control during treatment. Without sputum control, it is difficult to make sure that patients are ready to proceed to the continuous stage of treatment, especially for those with smear-positive TB. This could create problems in the future by increasing multi-drug resistance for those who are not fully cured.

10.6 Impact of the shortage of financial support for implementation of the DOT program

Although the MoH and NTP have put great effort into the TB and DOT program by providing free treatment to every patient, the problem still exists of insufficient financial support for the implementation of DOT. It was evident from the qualitative interviews that most HCs did not have enough financial support from NTP to cover TB education programs in the community; and in particular there was not enough funding for staff's transportation fees to visit patients in the community, or to transport sputum samples.

These problems could be more serious for HCs with CDOT, as the CDOT program was based on the availability of sponsors, and some HCs have withdrawn the program because of the shortage of sponsor funding. The majority of staff said they could not go often to visit CDOT patients in the community because the financial support for transportation was limited; also the incentive for DOT watchers involved in the CDOT program was very small. The insufficient financial support caused discouragement of staff and DOT watchers involved in the program implementation. This may explain some of the problems raised by patients such as the lack of follow-up activity by HC staff, and in some cases the absence of DOT watchers during treatment, which could affect patients' adherence to treatment. Moreover, the detriment to the CDOT program due to shortage of

funds from sponsors could reverse the implementation of the program and harm people in the community; for this reason some patients have changed their treatment location from the community to the HC.

Key Message: the seventh conclusion of the thesis is that there is insufficient financial support for the implementation of both HC-DOT and CDOT in Cambodia. This could create several problems in the implementation of DOT such as: TB case finding not achieving the target, increasing patient's non-adherence to treatment, and increasing the number of self-administration patients. In particular this problem is more serious for the CDOT program as it requires more follow-up and monitoring from staff at the HC level, as well as NGO funding for the DOT watchers.

10.7 The challenges of implementation of ambulatory DOT (HC-DOT)

Overall, the implementation of HC-DOT in Cambodia appears to be pretty successful in keeping the treatment success rate above the WHO target and in reducing the death rate due to TB. Based on the qualitative study, there were several factors, such as the involvement from staff and community health volunteers that played an important role in the achievements of this approach. Moreover, using health volunteers to observe patients taking medicines was also used in HC-DOT areas, especially for the continuous phase and for those patients who could not attend for treatment at the HC.

However, there were several issues relating to the implementation of HC-DOT found in this study. These issues were similar to those noted in previous studies in developing countries (Nair.D, George.A et al. 1997; Harper M 2003; Sanou A 2004). The first issue is that the HC-DOT treatment incurred travelling costs and time off work for patients who

needed to attend the HC everyday for at least two months of treatment; for this reason the majority of patients treated with the HC-DOT came to take medicines with staff at the HC for only the initial phase; the rest of treatment they were allowed to take at home. This confirmed the results of studies in Pakistan ((Khan A 2000; Khan M 2005). The second issue is the long waiting time for taking medicines with staff at the HC. The third issue is the difficulty in attending the HC for patients who are very sick or unable to come to the HC every day due to lack of transportation. The last issue is the lack of flexibility and patient choice in selecting the location and the DOT watcher during the treatment.

In contrast to previous studies by Jaiswal (Jaiswal A 2003) and Greene (Greene 2004), this study found that staff at the HC did put considerable effort into supporting patients to complete the treatment; most patients were very happy with the staff's attitudes which also influenced patients to come to the HC every day; this difference might be due to differences in culture and settings between the studies.

Although the issues above relating to the implementation of HC-DOT were raised and recognized by most patients in the study, when the author asked if they wanted to change the mode of treatment by switching from the HC-DOT to CDOT approach for their future treatment, many of the respondents would not have wanted to change because they were happy to be treated by staff at the HC. They felt that HC staff could help in motivating them to complete the treatment; in particular staff could help them to reduce any problems with side-effects. Some patients appreciated the fact that there was flexibility around their attendances at the HC and medicines were allowed to be taken at home during the weekend, on public holidays and on the request of patients. Patients also said

that they did not trust the qualification of DOT watchers as they were not medical professionals.

Key Message: the eighth conclusion of the thesis is that HC-DOT in Cambodia is flexible in some areas. Although there are some issues relating to the implementation of the program, it is generally acceptable to most patients. Satisfaction with the program was particularly high for patients who lived close to, or had easy access to the HC during treatment.

10.8 The challenges of implementation of CDOT

The main purpose of implementing the CDOT program in Cambodia was to remove the limitation and barriers caused by the ambulatory DOT as mentioned above. All interviewees in the qualitative study agreed that the CDOT program could help patients to cut their expenditures on travelling by reducing their visits to the HC; it could also help patients save time and allow them to engage with their normal daily activities, important for both patients and their families. Moreover, the CDOT program was seen to be very convenient for patients who were very sick, disabled or had difficulty accessing the HC. Results of this study confirm the results of previous qualitative studies by Wandwalo and Kabongo (Wandwalo E 2006; Kabongo D and B 2010). The level of adherence to treatment is increased for patients treated in the community because of convenience in terms of time and place. The study results also suggest that the CDOT program increased TB awareness and reduced TB stigmatization among people in the community, because people began to understand that TB is an infectious disease which can be cured by taking medicines regularly for 6 months, rather than being genetic.

However, several limitations of the CDOT program are apparent from this study; the first problem is the lack of incentives for CDOT watchers, which could impact the absence of DOT watchers during treatment. The second issue is the question of DOT watchers' ability; even though the majority of patients were happy to be treated by DOT watchers in the community, some patients complained that the information about treatment provided by DOT watchers was insufficient, compared to that of staff at the HC; in particular problems relating to side effects were not always dealt with effectively. Additionally, sometimes the dosage of medicines given to patients were incorrect since DOT watchers decided to reduce or increase the dosage without discussing this with HC staff. The third limitation is the lack of flexibility in selection of individual DOT watcher for or by patients. Many patients were not happy because HC staff had not allowed them to choose their own DOT watchers. The last limitation is that the environment for the CDOT program is not always as strict as the HC-DOT because of the more informal relationship between patients and DOT watchers. These problems have also been reported in other studies (Escott S 2005; Wandwalo E 2006; Kabongo D and B 2010; David K. Mafigiri, Janet W. McGrath et al. 2012).

A. Supporting the DOT watchers

The major weakness is the insufficient financial support for DOT watchers. As explained by Kironde (Kironde S 2002), for the success of CDOT program in the long term, the issue of sustainability of DOT watchers must be addressed; the most important issue is adequate financial incentives for DOT watchers and other community volunteers. Another review by Kangovi (Kangovi S 2009) showed that the CDOT programs which offered financial incentives to DOT watchers were likely to produce better outcomes, and to result in higher TB case finding. Providing proper financial support to the CDOT

program could provide staff at the HC with an opportunity to monitor and support CDOT watchers through team meetings, and spot checks by staff at the HC, rather than simply requiring CDOT watchers to fill out treatment cards. Providing a financial incentive could also help to motivate CDOT watchers in their job to spend more time on TB education for people in the community, finding more suspect cases, and supervising patients more strictly. Another interesting point raised by Kangovi is that CDOT programs which do not provide financial incentives to DOT watchers tend to utilize a family member as the DOT watcher, often chosen by the patient.

Most CDOT programs are implemented in developing countries where resources are constrained, so financial support for CDOT watchers is almost always insufficient. However, it is noted that lack of resources does not always constitute a barrier to success in the implementation of CDOT program. Studies by Manalo in Manila (Manalo F 1990) and Walley in Pakistan (Walley J.D 2001) showed that their DOT watchers did not receive any financial incentive from CDOT programs, but still provided good services to CDOT patients; the defaulters and case detection rates were improved after implementation of CDOT. In my study, too, it was clear that many DOT watchers gave generous care well beyond their financial rewards. DOT watchers may be motivated not only by financial incentives, but there is also non-financial support such as provision of free health care to DOT watchers and their family as well as the feeling that they are helping fellow villagers in the community. Providing a non-financial incentive to DOT watchers could be a good strategy to supplement CDOT programs with scarce resources, like Cambodia. It was observed in this study that DOT watchers also operated in some HCs which implemented only ambulatory DOT, and also in some HCs where the CDOT program had been formally terminated, although they were not paid to do so.

Key Message: the ninth conclusion of the thesis is that providing support for DOT watchers is the key to making the CDOT program successful in the long-term. Like other developing countries, Cambodia does not have enough financial resources to fully provide for DOT watchers, thus non financial support could be applied for CDOT program.

B. Providing proper training for DOT watchers

The issue of CDOT watchers' ability could be addressed by providing them with proper training, regular updating and follow-up of their work. Most CDOT watchers mentioned that the information about TB training and treatment received from HC staff was not enough and out of date. Regular meetings occurred only at the beginning of their work and feedback from staff was rarely received. This could explain why the information and dosage of medicines given to patients by CDOT watchers were sometimes inappropriate. Results from the qualitative study showed that CDOT watchers were the first people CDOT patients would seek out for help during treatment. It is of the utmost importance to provide them with the correct information about DOT treatment.

Key Message: The tenth conclusion is that CDOT watchers should receive appropriate and up-dated training in order to address the problem of CDOT watchers' capability in the CDOT program. Regular meetings, follow-up and feedbacks from staff should take place frequently in order to ensure that the correct treatment is given by CDOT watchers.

C. The selection of patients' treatment supporters

The experience of the CDOT program in Swaziland reported by Escott (Escott S 2005) may be relevant to the setting in Cambodia; he reports that the successful implementation

of CDOT requires many factors and the involvement from all parties including HC staff, DOT watchers, family members, and people in the community. The first factor is the patient's flexibility and the choice of individual treatment supporter. This is confirmed in my study; some of both the ambulatory and CDOT patients in the study wanted to be involved in the selection of their own DOT watchers; and sometimes family members would be more likely to be selected by patients as their treatment supporters. This study showed that family members already play their role as DOT watchers and reminders, especially for self-administration patients by giving medicines, reminding patients to take medicines, collecting medicines from the HC, and motivating patients to complete the treatment.

In general, the discussion still continues as to whether family members are suitable for supervising patients for CDOT programs. The argument was made for using family members as DOT watchers because it may improve patients' adherence to treatment; a study by MacIntyre (MacIntyre CR 2003) showed that the use of family members as DOT watchers resulted in worse adherence to TB treatment in a home-based DOT program. However that study was conducted in a developed country- Victoria, Australia.

Although in Cambodia family members are not recommended in the national guideline to be DOT supporters, in fact they have operated as such for both CDOT and HC-DOT patients. Moreover, this study found a lot of "non-DOT" (self administration) patients in both HCs; most of these revealed that their family members were their DOT watchers and reminders during their treatment. However, some of these patients still had TB symptoms and wanted to restart their treatment. Thus, the results from the qualitative study might partly explain the quantitative results as to why treatment outcomes in the CDOT

program were similar to HC-DOT, as family supervision and self-administration occurred in both HCs, and could impact the treatment success of both DOT approaches.

However, other studies conducted in developing countries have shown that using family members as DOT supervisors in the CDOT program can lead to good treatment outcomes (Nyirenda TE, Harries A.D et al. 2003; Mafigiri D 2007; Thiam S. 2007), and good adherence to treatment (Manders A.J.E, Banerjee A et al. 2001; Wandwalo E 2006; Kabongo D and B 2010) and can be as effective as other DOT supporters (Banerjee A 2000; Wright J 2004; Mathew A 2005; Newell JN 2006; Anuwatnonthakate A 2008). However it has also been shown in these studies that for the successful involvement of family members in CDOT program good training, monitoring and follow-up by staff at the HC are required.

Key Message: Based on the results of this study and experiences from various studies in different settings, family supervision could be applied to patients who are not able to come for the treatment at the HC, especially when no DOT watchers are available in the place where the patient lives. In order to avoid patients' non-adherence to treatment, staff need to put more effort in providing training, monitoring and frequent follow-up to family members employed as DOT watchers.

D. Selection of patients for CDOT program

The CDOT program may not be suitable for every patient; for example re-treatment patients, those who are too sick to walk to the DOT watcher's house, and those who live near to the HC may not be suitable. In Cambodia, in some areas the CDOT program is sponsored by NGOs which provide relatively good financial support and incentives to staff at the HC or CDOT watchers, such as providing money for transportation fees; in

these areas all appropriate patients could be registered by staff to have the treatment with the CDOT program. The qualitative study showed that the distance between some patients' houses and the DOT watcher's houses was further than the distance to the HC, while others said the distance between their home and the DOT watcher's house was the same distance as their home to the HC, but patients were allocated by staff to take medicines with DOT watchers in the community although this was not their preference, nor the more appropriate setting. This study also identified three patients who were inappropriately treated with the CDOT, as they were re-treatment patients; these patients should have been treated at the HC or the referral hospital, because the re-treatment regimes should involve daily streptomycin injections for the first two months. The implementation of the CDOT program would be more successful if the program was targeted to the right group; for example, those who live far from the HC and do not have transportation, or those who have a good reason why they could not come to the HC every day during the treatment. The CDOT program may not be appropriate for those who live close to the HC, or those too weak to walk to the DOT watcher's home who would be better having the treatment at home supervised by a family member who receives appropriate training from staff at the HC.

Key Message: the twelfth conclusion of the thesis is that identification of patients for whom community based care is appropriate must be clearly set out and implemented. The success of the CDOT program depends upon the implementation reaching the right targets and the right places.

10.9 The acceptability of implementing CDOT program in Cambodia

The CDOT program was well accepted by most CDOT and HC-DOT patients, DOT watchers and some staff in both HCs. They recognised that CDOT could remove or

reduce many barriers such as inconvenience, and travelling costs to patients, and could allow patients enough time to engage with normal daily activities. CDOT is particularly convenient for those who are sick and have difficulty in coming to the HC every day. Most CDOT patients were satisfied and very happy to have DOT watchers in the community because their DOT watchers were known to them and helped and motivated them to complete the treatment.

In contrast many staff in HCs both with and without CDOT questioned the effectiveness of the CDOT program and DOT watchers' capability in supervising patients in the community. Many of them expressed concern about the shortage of financial support for DOT watchers and lack of follow-up from staff at the HC, which could cause failure of the program. Most staff recommended the CDOT program as more appropriate for the continuous phase, when medicines are given to patients to take in the community.

On the other hand, the HC-DOT was considered satisfactory by some HC-DOT patients and staff, because they felt that the HC-DOT was already as flexible and convenient as the CDOT program and HC staff were the best people to advise and motivate them to complete the treatment. This may be because the implementation of HC-DOT in Cambodia is already very successful for most patients.

Key Message: The last conclusion of this thesis is that the two approaches are complementary rather than alternatives. Implementation of HC-DOT in Cambodia is generally considered to be successful by staff and patients, and the implementation of CDOT is also acceptable among most patients and DOT watchers in the community, especially where the HCs are located far from the patients' houses. It is important therefore to identify the mix and criteria for offering each

option. Although this study did not aim to assess self care, evidence from the qualitative study suggested that this was more likely to result in serious problems of disease recurrence for non-DOT patients.

10.10 Limitation and strengths of the study

A. Strengths of the study

The strength of this study is that it is the first such study in Cambodia conducted using both quantitative and qualitative methods to examine the effectiveness and acceptability of CDOT compared to the existing HC-DOT and to find out the gaps and issues in the implementation of both DOT approaches in the field by HC staff, patients, and DOT watchers. Moreover, before this study was conducted in Cambodia, the author carried out a meta-analysis of the effectiveness of CDOT programs compared to HC-DOT globally, to determine the comparative effectiveness of CDOT programs in different settings. The author also carried out a pilot study in four HCs, to assess the real design effects for the quantitative study, to examine the data quality, to pre-test the qualitative study tool, and to allow a better understanding of the complex environment of the HC and patients in the community. The pilot therefore strengthened the design and appropriateness of the main studies.

Despite this being a before-after implementation study rather than a RCT, the coverage was broad as the HCs selected for the study were 81 HCs in 21 provinces out of the 24 provinces in Cambodia, this representing the whole country. In particular, the HCs selected where the HC-DOT and CDOT were implemented were in the rural areas where the infrastructure as was very weak. The sample size of this study is 2700 patients, which is comparable to the previous study by Becx-Bleumink (Becx-Bleumink M 2001) (2353

participants). All data entry was double-checked by two official statisticians. The analysis in this study was carried out separately for all types of TB and for new-smear positive TB and the comparison of treatment success was analysed before and after the introduction of the CDOT program as well as between areas where the program was and was not implemented.

Furthermore, the qualitative study provided wide ranging, detailed information about the strengths and weaknesses of each DOT option and how they operated in the field from the experiences of patients, staff and DOT watchers in the implementation of each approach.

B. Limitations of the study

The main design of the quantitative study is a before and after intervention study. This is a quasi-experimental study of before and after implementation of the program, in a group that received the intervention compared to a control group that did not. As this is not a randomised controlled trial it has some limitations such as: patients selected into the study were not randomised, the data are reliant on records from the HC registers to determine the outcomes, and external influences that may have induced changes in both areas could not be measured. However, to minimize these limitations, the comparison of baseline data in both areas were also analysed and differences from baseline data taken into account; the patient's treatment cards were also verified by the researchers to determine whether the data were missing from the register. Additionally, to minimize the effect of missing data 10% was added for the sample size calculation. There was no difference in "missingness" between the groups.

Another limitation of the quantitative study is selection bias of HCs into the study. Firstly the choice of HCs which implemented CDOT were almost certainly not random, as we know that these tended to be HCs with relatively poor baseline results. This again may result in an underestimate of the relative benefit of CDOT. There is another potential bias due to the fact that the selection of HCs which implemented CDOT in the study was based on the existing HCs where CDOT was ongoing; 41 HCs where CDOT was withdrawn in 2005 were excluded from this study as this would have involved a third group. This bias may have impacted on the estimation treatment success rates for CDOT areas; the odds ratio for treatment success for CDOT might be overestimated if CDOT was withdrawn due to unsatisfactory performance. However the outcomes may have been unaffected in the more likely cases where implementation of CDOT programs was discontinued because of failure of the program due to lack of funds.

A further limitation is the issue of selection bias and information bias in the qualitative part of the study. As discussed above, some patients were selected by convenience sampling and by recommendation of the DOT watchers or staff at the HC due to the poor road conditions, the migration of patients, and the absence of patients during the author's visits. This bias could impact on the findings related to patients' adherence to treatment, and as a result the findings on support by DOT watchers or staff to these patients would be overstated. Since some patients were selected based on their housing location, such as patients who lived close to the main road or the HC; so the level of adherence to treatment may be higher than those who lived in very remote areas and difficult to access to the HC. This may have understated problems for HC-DOT patients. Moreover, the author could not interview defaulter patients where they had moved out of the villages; it would be interesting to know the reasons why they did not complete the treatment.

Although the author explained the study to participants, information bias could have affected the interviews, since participants may have thought that the study was conducted by the HC or the government. Participants may not have always answered questions honestly, since Cambodian people tend not to criticise public health services out of respect for staff from the government. This bias may lead to an overestimate of the positive aspects of the staff attitudes and the health service system. Participants may have provided only positive comments on the health service system and staff's behaviors.

Patients selected for interview in the qualitative study had mostly finished treatment more than six months ago; patients may not have recalled some information regarding the treatment and sputum control, or how many times they collected medicines from the HC, or how often staff came to visit patients in the community during the treatment. It may have introduced errors in information on systematic of DOT administration and treatment guideline provided by the NTP.

The last limitation is that this study does not assess the cost or cost-effectiveness of CDOT program in particular costs to the health care system for patient treated with CDOT and ambulatory DOT. This is due to limits of the time frame.

10.11 Recommendations

The evidence from both quantitative and qualitative studies showed that the effectiveness of both HC-DOT and CDOT were not significantly different; both were seen to maintain high treatment success rates and improved TB case findings over the period studies. Both HC-DOT and CDOT were generally working well and were acceptable among most patients, HC staff and CDOT watchers; most patients were happy with their DOT

approaches. Findings of this study showed that CDOT was convenient for patients with disability or having difficulty to access the HC, or needing the time to work. Moreover, CDOT could not be implemented alone and should not replace the existing HC-DOT, both HC-DOT and CDOT are complementary and between them fulfil different needs. However, there are some major problems that need to be addressed with the current resources and with long term funding in order to maintain and improve both DOT approaches in Cambodia. These include the allocation of patients to ambulatory DOT or CDOT, the selection of DOT watchers, the need for up-to-date training for CDOT watchers, speeding up the process of sputum tests, providing incentives for CDOT watchers, and providing sufficient resources for HC staff to visit patients and educate people in the community.

A. Allocation of patients to ambulatory DOT or CDOT

Both DOT approaches would be more successful if the implementation reached the right targets and right places. CDOT would seem to be essential for people who are very sick, unable to come to the HC, patients living far from the HC, and patients who need to work. Ambulatory DOT would seem to be convenient for people who live close to the HC. However, HC staff should discuss more with patients where they want to be treated and reasons why they select that option before starting treatment.

B. The choice of selecting the individual DOT watcher

Because selection of DOT watchers may impact the patients' adherence to treatment, patients for TB treatment should be allowed to play a part in selecting the DOT watcher. In this study, besides the community health volunteers, family members were found to be acceptable and appropriate for some patients. In Cambodian culture, especially in rural

areas, family members have the obligation of taking care of sick people especially for chronic diseases such as hepatitis, HIV/AIDS and also TB. Family DOT should be employed for some patients who are really sick and where there is no availability of health volunteers where the patient lives. With the current situation of financial support for CDOT program in Cambodia, employing family DOT for some patients would reduce the financial burden of the program. However, using family members as DOT watchers would not be recommended for general patients since family DOT may not supervise patients as strictly as HC staff or CDOT watchers. The family members employed as DOT watcher would need to be properly trained and monitored by HC staff for TB education and the DOT treatment process.

C. Providing up to date training and feedback for CDOT watchers

The issue of the CDOT watchers' ability could be resolved by HC staff providing sufficient training for them, including providing up-to-date information about DOT treatment, providing feedback and regularly following-up their work in the community. Providing more training and follow-up needs more funds, however, this training and feedback could be integrated with other health promotion activities when health volunteers come for training at the HC.

D. Speeding up the process of sputum tests

Delay in receiving the test results was a major problem in both HCs. Speeding up the sending and return of results for sputum tests would mean that treatment could be started earlier and indicate whether the intensive phase should continue or the continuous phase should stop and in particular it would give greater certainty as to whether a patient was cured or not. This could be achieved in several ways. Firstly given limited funds, the

treatment card should have the date, month and year when patients need to come for the sputum test at the HC. Since the result of the tests take between one and two weeks, it would be necessary for patients to come for the control test one week before the intensive phase finishes. Both ambulatory DOT and CDOT patients should come for sputum tests by themselves where possible because this could avoid the effects of any poor technique of collecting sputum by CDOT watchers. Reminding patients of the date of the control test should be done by HC staff or CDOT watchers. Secondly, if funds were available, each HC could have at least one microscope for reading the sputum tests. Most TB staff mentioned in the study that they have been working in TB units for more than five years and some have experience as staff at the laboratory. However, training in reading the sputum test could be provided by the CENAT and MoH to TB staff at the HC. Having their own microscope at the HC could reduce the transportation costs involved in sending sputum to laboratory and would speed up the process of sputum results.

E. Incentives in kind for CDOT watchers

Maintaining and sustaining the motivation of CDOT watchers is the key to successful implementation of CDOT. With the limited resources available, providing free health care to CDOT watchers' families like the current situation in Cambodia would be recommended; however, more incentives for CDOT watchers would be helpful in the long run. Providing sufficient funds for CDOT watchers to cover the transportation costs of collecting medicines and visiting patients at home should be considered, and this could possibly be discussed with sponsors before implementation of CDOT in every HC.

F. Improve TB health education in the community

Based on this study, TB health education and promotion in the community needs to be improved. Health education is a key component in increasing the patient's knowledge of TB and can motivate them to change their attitudes for TB treatment. This could be done through HC staff, health volunteers and CDOT watchers in the community. Providing sufficient resources for HC staff to visit and educate people in the village would be helpful also.

G. Feasibility of the CDOT program

The CDOT program is largely dependent on NGOs and available funding. There are several NGOs supporting CDOT, mainly USAID and the Global Fund, which have provided long-term funds normally between 3 to 5 years; as reported by the NTP at the end of 2010 the implementation of the CDOT program has expanded to 60% of HCs in Cambodia (MoH December 2010). This successful expansion of CDOT must come from the NTP putting more effort in looking for more sponsors including local and international NGOs. Although there are some problems with CDOT implementation where sponsors have withdrawn funding or given funds for limited period, the program is still pretty successful and could expand if the government sought more sponsors to implement the program.

H. Providing supports for patients

Continuation of the food gifts to patients during treatment is strongly recommended because it both encourages patients to complete their treatment and also improves their nutrition, which is likely to aid recovery. Poor nutrition is one of the key factors in increasing the risk of TB.

I. Treatment guidelines

Treatment guidelines need to be clear, but more flexible in the interests of patients and HC staff. For example, they may need to be adjusted to acknowledge where patients can take medicines during weekends and holidays, because staff would not be present at the HC then. This flexibility is especially important in relation to the location where ambulatory patients can take medicines for the continuous phase, as there is a risk that many patients self administer at this stage.

J. Future research on the cost-effectiveness of CDOT program

Studies conducted in other settings have indicated that CDOT reduced costs and was cost-effective compared with HC-DOT (Floyd K 2003; Wandwalo E 2005). Considering future research, the author would strongly recommend assessing an integrated service together with a cost analysis. This would help policy makers determine how the CDOT programme should be funded nationally or whether they should look for further NGO funding. Similarly it would be useful to determine the role of "family DOT".

Appendix 1: Combinations of search terms and concepts used to locate relevant studies in Pubmed, CINAHL, EMBASE and CENTRAL

Search Terms	PubMed	CINAHL *	EMBASE*	Cochrane Central Register of Controlled Trials
1. Tuberculosis				
2. Directly Observed therapy (DOT)				
3. 1 & 2	√	√	√	√
4. Health facility based DOT or (health center DOT)				
5. 1 & 4	√	√	√	√
6. Community based DOT				
7. 1 & 6	√	√	√	√
8. 1 & Community involvement	√	√	√	-
9. 1 & patients' adherence	√	√	√	-

♦ Search terms used in combination with the search strategy for retrieving trials: upper case MeSH or Emtree: heading lower case: free text term.

Searches were conducted from 1995 until 2012 because DOT has been fully implemented only since 1994. The key words tuberculosis and TB were combined with keywords about, using keywords “tuberculosis, directly observed therapy DOT, community based DOT, community involvement, health centre DOT, health facility based DOT, and patients' adherence”. Hand search of the International Journal of Tuberculosis and Lung Disease was carried out from 1995 to 2012. Also searched were published bibliographies of related topics, and citations in articles which were included in this review.

Appendix 2: Summary of included studies the effectiveness of CDOT compared to alternative DOT options

Year of publication of study	Country	Objectives	Setting	Methods	Sample size	Form of TB	Treatment supervisor	Results
2000(Zw arenstein M 2000)	Cape Town , South Africa	Compare the successful of tuberculosis treatment outcome rate between self supervision, supervision by lay health worker (LHW), and supervision by clinic nurse	Suburb	<ul style="list-style-type: none"> - Unblinded randomized control, trial - 3 arms were assigned in the study. - The first group is self supervised which patients took medicines at home and visited the clinic once a week, or sent a family member to collect their 	156 TB patients	Adult aged over 15 years, pulmonary TB patients(new and retreatment)	Community health volunteer	<ul style="list-style-type: none"> - There were no significant differences in successful treatment rates across the three supervision (P=0.136) - LHW supervision outcomes, over all patients, were not statistically significantly superior to either clinic DOT (17.2%, 95%CI:-0.1-34.5) or to self supervision (15%, 95%CI:-3.7-33.6) - Clinic and self supervision outcomes were similar to each other (-2.2%, 95%CI:-21.5-17.1) - New patients benefit from

				<p>drugs during the period of treatment</p> <ul style="list-style-type: none"> - The second group is the group who patients received supervise by the LHW - The third arm is patients who received the supervise from staff at the clinic 				<p>LHW supervision (LHW vs clinic nurse: risk difference 24.2%, 95%CI:6-42.5, LHW vs self supervision 39.1%, 95%CI: 17.8-60.3) as do female patients (LHW vs clinic nurse 48.3%, 95%CI:22.8-73.8, LHW vs self supervision 32.6%, 95%CI: 6.4-58.7)</p>
2003(Fred L 2003)	Kilombero /Tanzania	<ul style="list-style-type: none"> - Evaluate the efficacy of community-based vs institutional-based DOTS - Compare the 	Rural/f arm with low income	<ul style="list-style-type: none"> - Unmasked cluster-randomized control trial - Intervention group is 	522 TB patients	New smear-positive pulmonary TB	Community volunteers	<ul style="list-style-type: none"> - The cure rate for patients under community-based DOT was similar to patients under health facility-based DOT - Community-based DOT

		effect of the two strategies during the intensive treatment phase		received a community member observed the patient daily during the first two month				may be a viable alternative to health facility-based DOT - Community-based DOT may be particularly useful in parts of the country where people live far from health facilities
2004(Eliud W 2004)	Tanzania	Evaluate the effectiveness of community-based DOT compared to hospital-based DOT	Urban	- Unblinded randomized control trial - Intervention group is group of patients who were assisted by guardian or, in his/her absence, a former TB patients	587 TB patients	All forms	- Guardian was defined as a family member or a close relative living with the patients - Former TB patients	- Success treatment outcomes for patients under community-based DOT and health facility-based DOT were similar: 85% and 83% respectively - Percentage of patients felt to submit sputum at the end of treatment was high in community-based DOT (9.8%) compared to once under health facility DOT (3.4%) - Community-based DOT is

								as effective as health facility-based DOT and can achieve good treatment outcomes
2004(Singh A.A 2004)	North India/ Haryana	Evaluate the effectiveness of urban community volunteers in using DOT	Urban	Unblinded randomized control trial with intervention group who is received supervise by community volunteers	617 TB patients	New smear-positive pulmonary TB	- District providers not employed as government health workers - Urban community volunteers such as shoe-shop owner, a temple priest, practitioners of traditional, welfare clinic staff, and teachers	- The proportion of total patients treated under community DOT increased significantly from 13% in 2000 to 25% in 2002 - The treatment success rate among patients treated by community DOT was similar to that among patients treated by health facility DOT (78% vs 77%) with the cure rate 70% vs 75%
2005(Nirupa C)	Tiruvallur/ India	Assess treatment outcome and	Rural	Unrandomized control trial	3019 TB patients	New smear-	- Government health workers	- Treatment success rate treated by different DOT

2005)		problems encountered by patients managed by different DOT providers in RNTCP		
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	<p>positive pulmonary TB</p>	<p>at primary health institutions (PHIs)</p> <ul style="list-style-type: none"> - Government outreach workers - Non-governmental sectors: Anganwadi workers, community volunteers 	<p>providers were similar: Anganwadi (80%), government outreach workers (81%), community volunteers (76%), PHI staff (76%)</p> <ul style="list-style-type: none"> - Patients treated by community volunteers and PHI staff had high default rate (18% and 17%) - Monitoring TB activities report was poor among supervision of Anganwadi and community volunteers while the government staff had a monitoring activities through weekly review meetings - Community volunteers and Anganwadi workers had a minimal training in
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								health related issues and side effect of TB medication
2005(Cla rke M 2005)	Boland health district, Cape province, South Africa	Evaluate the effect of lay health workers (LHWs) on tuberculosis control among permanent farm workers and farm dwellers in an area with particularly high TB prevalence	Rural/f arm area	- Unblinded cluster randomized control trial - Intervention group is group of patients who were chosen to receive DOT from the LHW, who has received the TB training from the nurse at the clinic - Control group is group of patients who received the	211 TB patients	- All TB forms, new patients and retreatment patients Multidrug- resistant TB patients were excluded	Lay health workers	- The successful treatment completion rate in new smear positive adult TB patients was 18.7% higher on farms in the intervention group than on farms in the control group (P=0.042, 95%CI:0.9-36.4) - Case finding for adult new smear positive TB cases was higher on farms in the intervention group compared to the control group (P=0.2671)

				standard TB treatment				
2009(Daniel G. Datiko 2009)	Sidama/Southern Ethiopia	Establish whether involving health extension workers (HEWs) in TB control improved smear-positive case detection and treatment success rates in Southern Ethiopia	Rural District	- Unblinded cluster randomized controlled trial - Intervention group: patients treated under supervised by HEWs who were health workers and health volunteers, who received the training for TB education and DOT such as symptoms, transmission of TB, how to	318 participants	Smear-positive TB	Community health workers/health volunteers	-The mean for case detection rate was higher in the intervention (122.2% vs 69.4%, $p<0.001$) and for the female patients (149% vs 91.6%, $p<0.001$) - The mean for treatment success rate for females was also high in the intervention than control (89.8% vs 81.3%, $p=0.05$)

				<p>identify TB suspects, how to collect, administer DOT and follow-up patients during the treatment</p> <p>- Control group: patients received the standard DOT at the HC, which supervised by health staff</p>				
2001(Bek x-Bleumin k M 2001)	Sulawesi, Indonesia	Compare of TB case notification and treatment results in a community based tuberculosis	Rural	<p>- Before and after study</p> <p>- The base line was collected in 1996-1997</p>	2353 TB patients	New smear-positive TB	- 1998 the community based TB program (CBTP) was introduced in	- Comparing the case notification between villages with CBTP and the non-CBTP villages, in 1998 the rate more than tripled to 166 (51,68 in 1996 and

		<p>programme(CBTP) , before and after introduction of the programme and between areas where the programme was and was not introduced.</p>		<p>before the introducing of community participation in TB. - The data was collected in 1998 when the community participation was introduced</p>	
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	<p>224 of the 772 villages of two rural areas in Sulawesi.</p> <ul style="list-style-type: none"> - Villages which implemented CBTP, health center need to provide health education and information to the leaders including the village heads, religious leaders and member of Women's association group. - Sub- 	<p>1997) in the CBTP villages, and increased slightly to 70 (62, 60 in 1996 and 1997) in the non-CBTP villages.</p> <ul style="list-style-type: none"> - The sputum conversion results at the end of the first 2 months, for the base line (1996-1997) the convention rate was higher in the CBTP villages but the difference was not statistically significant. But in 1998 the conversion rate was significantly higher in for patients treated in the CBTP villages. - The treatment success rate (cure + treatment completion) was higher in the CBTP than in the non-CBTP villages. For the
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							<p>center health workers and village midwives were selected and trained by HC staff. They were responsible in following up patients to complete treatment.</p> <p>- A household member was required to observe patients taking medicines at home</p>	<p>1996-1997 the difference was not statistically significant, but for 1998 the treatment success rate was significantly higher in the CBTP villages.</p> <p>- The decline in failure rate in both the CBTP and the non-CBTP villages was statistically significant.</p>

2002(Kir onde S and Kahirimb anyi 2002)	Northern Cape/ South Africa	Explore the feasibility of community participation in a high-burden Tuberculosis Control Programme and establish how supervision of treatment by lay volunteers compares with other methods of tuberculosis treatment delivery	Rural/ Urban	- Prospective cohort study - The intervention group, patients were treated under community- based DOT and assigned to lay volunteers as DOT supporters. DOT supporter has received the training about supervising, recording and follow-up patients from nurse at the	595 TB patients	Pulmonary TB	-Lay volunteers for the intervention - Clinic nurse for the control group	- There was no significant difference in the treatment success between community-based treatment supervision and clinic- based DOT (P=0.367) - Only 54% of retreatment patients has a successful treatment outcome compared to 70% of new patients. This difference was found to be statically significant (p<0.001) - Almost 93% of DOT supporters were female. 70% of DOT supporter were less than 45 years of age - The DOT supporters were significantly more educated than the TB patients (X ² =60.37, P <0.001)
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				<p>clinic</p> <ul style="list-style-type: none"> - The control group, patients were treated with the clinic-based DOT. Patients were asked to come to the clinic five days a week to be observed by the clinic nurse - Questionnaire interviews were also carried out with 135 lay volunteers participating in the TB program 				

2003(De missie M 2003)	North Ethiopia	Assess the effectiveness of “TB club” in improving compliance with TB treatment and their impact in improving societal attitudes associated with TB	Rural	<ul style="list-style-type: none"> - The study used both quantitative and qualitative - For the quantitative, prospective cohort study is used to compare the treatment outcomes between the intervention groups where patients received support from the “TB club”; and the control group where patients treated 	128 patients	New smear-positive pulmonary TB	<ul style="list-style-type: none"> - For the control group: health facility’s staff - For the intervention group: TB health workers 	<ul style="list-style-type: none"> - The treatment completion was significantly better in the TB club group (68.7%) ($X^2=5.41$, $P<0.02$) compared to the comparison group (46.8%) - The default rate was also significantly lower in the TB club group (12.5% ($X^2=11.57$, $P<0.001$) than in the comparison group (40.6%) - However, the difference in the death rates was not statistically significant ($X^2=1.09$, $p=0.29$) died in the TB club (17.2%) and the comparison group (9.4%) - According to the qualitative study, patients treated with TB club have
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				with regular TB care in health facilities - For the qualitative study, focus group discussion and an in-depth interviewed are conducted				better knowledge for TB education and treatment
2003(Aro ra V.K 2003)	New Delhi/ India	Determine feasibility, acceptability and efficacy of domiciliary DOTS execution to TB patients through services of community DOTS providers	Urban	Prospective cohort study	3127 TB patients	All forms	Community volunteers/ neighbors	- Overall treatment success under community-bases DOT was significantly better than the other patients treated at health facility DOT - TB knowledge among patients treated under community DOT was better than once treated at health facility

									- Community DOT was able to carry out of successful in TB care and acceptable in the community
2003(Du dley L 2003)	South Africa, Cape Town	Evaluate community treatment supervision as part of tuberculosis programme implementation	Urban settlements/ low income	-Non-randomized prospective study - Intervention area (Guguletu) where patients receive the community-based TB care - For the control area (Nyanga), patients receive with only health facilities TB care	2873 Adult TB patients	All form	TB	-Community Health Association of South Africa (CHASA): community health workers for the intervention area - Nurse or clinic staff for the control area	- Community supervision had a better outcomes for both new patients (P<0.05) and retreatment patients(P<0.05) - The cure rate for new smear positive patients on community supervision was higher than for patients on clinic supervision (72% vs 46%); and the interruption rate lower (13% vs 25%) - For retreatment patients the cure rate was also higher (63% vs 35%) and the interruption rate lower in the intervention area

								(18% vs 30%) - Case finding in the intervention area was also higher than control area
2007(Khi eu K 2007)	Cambodia	Compare the results of TB treatment between health center-DOT and community-based DOT	Rural	- A retrospective cohort study - The intervention group: patients received DOT under the community -The control group: patients treated with the HC-DOT	1269 patients	All TB forms	- For CDOT: community health workers - For HC-DOT: staff	- There is no significant difference for cure rate between HC-DOT and CDOT (90.2% vs 92.5%) - There is also no significant difference for completed treatment in patients with smear negative pulmonary TB and people with extra-pulmonary TB for both HC-DOT and CDOT, completed treatment was 93.4% in HC-DOT and 96.2% in CDOT
2007(Ca valcante)	Rio de Janeiro	Compare community-based	Urban/ City	- A Retrospective	1811 patients	All TB forms	- Staff at the clinic such as	- Comparing the outcomes for slum residents, the

S.C 2007)	City, Brazil	directly observed treatment for tuberculosis using community health workers , with clinic-based DOT	cohort study which is compared two ways of implementing DOT program - The clinic- based program which is called control program, the treatment is taken place in the clinic where patients were supervised by a team including physicians and nurses - The intervention
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		<p>physicians, nurses, auxiliary nurses and outreach workers</p> <p>- Community health workers</p>	<p>overall success rates were higher for those treated with community-based DOT, followed by clinic-based DOT and self-administration treatment (90.4%, 82.1% and 75.8%)</p> <p>- The treatment success rate for all patients in the community-based DOT program was significantly higher than in the clinic-based DOT (90.4% vs 78.2%, $P < 0.001$)</p> <p>- Treatment success rates of new smear-positive TB and retreatment cases were also significantly higher among patients treated with community-based DOT</p> <p>- The default rate was significantly lower in</p>
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				program or community-based DOT, the treatment is taken place at the patient's home or at the church Patients were supervised by the community health workers				community-based DOT compared to the clinic-based DOT (4.7% vs 12.7%, P<0.001) - The acceptance of DOT was dramatically higher amongst patients treated under the community-based DOT (98.9%) than for those treated in the clinic-based DOT (60%, P<0.001) - Patients received community-based DOT were more likely to have successful treatment (OR=3, CI 1.9-4.8) than those who received clinic-based DOT (OR=1.5, CI 0.9-2.4)
2009(Bo ogaard van den J	Kilimanjaro/Tanzania	Assess the effect of the introduction of the patients-centred	Rural and urban	- A retrospective cohort study	2769 patients	All forms TB	- For CDOT: family members or	- Compared to patients under facility-based DOT, patients under community

2009)		tuberculosis treatment approach-which allows tuberculosis patients to choose between community and facility-based DOT –on treatment outcomes, and to analyze factors that contribute to opting for community DOT		which is compared two ways of implementing DOT program - Intervention group is that patients treated with CDOT - Control group is that patients treated with facility-based DOT			spouse - For facility-based DOT: staff at the clinic	DOT were more likely to be female, aged<15 years or HIV positive - Treatment success was more likely in patients under CDOT than in those under facility-based DOT (81% vs 70%), in patients with smear-positive pulmonary TB, and in patients who were HIV-negative - Cure rates did not differ significantly between patients who opted for CDOT and those who opted for facility-based DOT (73% and 72%, respectively; OR=1.1, 95%CI 0.8-1.4)
2010(Ka bongo D	Kweneng/ Botswana	Assess the outcomes of home-	Rural	- Combined method of	405 patients	All new TB types	-HB-DOT: community	- Overall, the treatment success rate was 83%.

<p>and B 2010)</p>		<p>based directly observed treatment (HB-DOT) versus facility-based DOT (FB-DOT)</p>	<p>quantitative and qualitative study</p> <p>- For quantitative e study: a prospective cohort study which is to compare the treatment outcomes between HB- DOT and FB- DOT</p> <p>- HB-DOT, <i>patients treated</i> with community health</p>
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		<p>volunteers or health education assistants</p> <p>- FB-DOT: nurses or staff at the HC</p>	<p>- The outcome of treatment did not differ significantly between of HB-DOT and FB-DOT ($p=0.45$)</p> <p>- The cure rate for patients with smear positive was also no different between HB-DOT and FB-DOT ($p=0.48$)</p> <p>- However, health workers in the FB-DOT performed better in effort to trace contacts of TB patients ($p<0.01$)</p>
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				<p>volunteers or health education assistants.</p> <p>Health volunteers were responsible in supervising patients taking medicines</p> <p>- FB-DOT, patients were supervised by nurses at the health facility</p>				
2011(André P. Gabriel 2011)	Kampala/ Uganda	Compare the treatment outcomes between the community-based DOT with clinic DOT	Urban	<p>-Prospective cohort study</p> <p>- The intervention: patients treated in the</p>	107 TB patients	Smear-positive TB	-Community health volunteers	- There was no significant difference in the treatment success rate between home-based DOTS and clinic-based DOT (OR=0.29, 95%CI: 0.06-1.34)

				community under supervised by health workers					
2006(Ne well JN 2006)	Nepal	Assess the success rates of two DOTS strategies	Rural	- Unblinded cluster-randomized controlled trial to compare two strategies- community DOTS and family-member DOTS - Intervention group is group of patients who treated with family-member DOTS - Control group is group of	907 TB patients	All TB forms	- Community DOTS: female health volunteers, health workers - Family-member DOTS: household members	- There was no statistically significant difference in success rates (cure and treatment completion) between the intervention and control group (89% vs 85%; OR= 0.67, 95% CI 0.41-1.10) - Estimated case-finding rates were 63% with the community DOTS and 44% with family-member DOTS	

				patients who received the treatment with community DOTS				
2004(Wright J 2004)	Lubombo, Swaziland	Evaluate and compare the effectiveness of direct observation by community health workers and family members	Rural	<ul style="list-style-type: none"> - Unblinded cluster-randomized controlled trial - Intervention group was supervised by community health workers - Control group was supervised by family members or careers who nominated by the patient and trained in 	<ul style="list-style-type: none"> - 1353 for all TB forms - 595 new smear positive TB 	All TB forms	<ul style="list-style-type: none"> - Community health workers - Family members or carer supervision 	<ul style="list-style-type: none"> - There was a non-significant difference in the cure and completion rate between the two groups (P=0.52, CI:3-7) - There was a non-significant difference in the cure and completion rates between female and male (P=0.06, CI:0-10) - The overall cure rate for new sputum smear positive was 65%, this number increased to 70% when cure and treatment completed rates were combined - For new smear positive,

				observing the patient take his/her medication		
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there was a significant difference between two groups for treatment success (cure + treatment completion) (7% difference, $P=0.06$)

- For new smear positive, there was a significant difference in cure rate between the two sexes ($P=0.002$, 12% difference, CI:5-20)

- Patients who were supervised with CDOT and family DOT showed the same success in treatment outcomes. However, there was a significant increase in successful treatment completion rates compared with before the DOTS programme was

								implemented
2008(Anuwatnont hakate A 2008)	Thailand	Evaluate the impact of different DOT strategies on TB treatment outcomes	Rural/Urban	<ul style="list-style-type: none"> - Prospective cohort study to compare two outcomes between patients supervised by health care workers and family member - Patients treated with the intervention group, were supervised by health care workers at the first two months(intensive phase) - Patients 	6625 TB patients	Pulmonary TB	<ul style="list-style-type: none"> - Health care worker (HCW) - Family member 	<ul style="list-style-type: none"> - At the end of treatment, patients who received HCW DOT were not significantly more likely to have treatment success compared with family DOT patients (OR =1.1, CI: 0.9-1.2) - If the analysis restricted to evaluate the impact of DOT on only default at the end of TB treatment, HCW DOT was strongly associated with treatment success compared with family DOT. - In patients that had treatment success or default at the end of treatment, 1,369(93%) of 1477 HCW DOT patients had treatment

				treated with the control group, were supervised by family-member who have received training about TB education, observing and recording ingestion of anti-TB medicine by public health staff				success compared with 3,130(89%) of 3,529 family DOT patients (OR 1.5, CI: 1.2-1.9)
2005(Ma thew A 2005)	Jharkhand State, India	Compare the completion rates of the two tuberculosis control programmes of the Nav Jivan Hospital,	Rural	- A retrospective cohort study which is compared two ways of	681 TB patients	All TB forms	- For the community-based DOT, DOT provider is the village health workers	- There is a significant difference between the completion rates of both programme (P<0.05) - The treatment completion rate of only 64.3% in the

		<p>Tumbagara, and to show that even in difficult areas, a DOTS programme can be successfully implemented</p>	<p>delivering a DOTS programme</p> <ul style="list-style-type: none"> - The control group where patients take the pills with family member supervised, go to collect drugs at the clinic once a month, and patients need to pay for the drugs (which is called DOST group) - The intervention group is group who use community 	
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		who is trained by DOT supervisor from the hospital	DOST group, while that in the intervention group was 89.2% - There was a non-significant difference in completion rates between new and retreatment patients ($P>0.05$)
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				based DOT program				
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Appendix 3: Summary and the reasons of excluded studies from this review

Year of publication	Objectives	Reason for exclusion
1990(Manalo F 1990)	Examine the treatment success by using community-based short course treatment of pulmonary TB	Report only the treatment outcomes under supervised by community health workers alone. Not comparing with other alternative DOT
1996(Dick J 1996)	Evaluate the effectiveness of the group of volunteers in enhancing adherence of notified TB patients to tuberculosis treatment	The main outcome was patient adherence to TB treatment. The treatment success was not given
1996(Dick J 1996)	Describes the perceptions of health team members regarding the voluntary community health worker project	Qualitative study
1997(Chowdhury A M R 1997)	Assess the treatment outcomes by using the community health worker as patient's supervisor in phase 1: 12 months treatment and phase 2: 8 months oral regime	Report only the treatment outcomes under supervised by community health workers alone. Not comparing with other alternative DOT
1997(Dick J 1997)	Describe and evaluate a lay worker project designed to enhance the effective control of tuberculosis in a rural/farm setting	The treatment outcomes were not given in the report
1997(David W and Geraint 1997)	Examine the successful use of voluntary lay people and community health workers in the delivery of community-based DOT	The treatment outcomes were not given in the report
2001(Walley J.D 2001)	Assess the effectiveness of different package for TB treatment under operational conditions in	Intervention group is mixed between staff at the HC and community health worker

	Pakistan	
2001(Manders A.J.E, Banerjee A et al. 2001)	Measure adherence to treatment of patients on guardian-based DOT, health centre-based DOT, and in-patient DOT during the intensive phase of treatment	The outcome measure was the adherence to TB treatment
2002(Pungrassami P 2002)	Compare the treatment outcomes between two DOT deliveries: hospital DOT and family DOT	Not community-based DOT
2002(Barker R.D 2002)	Illustrate successes and difficulties for the South African National Tuberculosis Programme in a rural area	Report only the treatment outcomes under supervised by community health workers alone. Not comparing with other alternative DOT
2003(Adatu F 2003)	Measure the effectiveness and acceptability of community-based TB care using the DOT strategy for TB control	Before and After study but no control group
2003(Miti S 2003)	Evaluate the implementation of the directly observed treatment, short-course (DOTS) strategy as part of an existing HIV/AIDS home care programme, by comparing TB treatment outcomes in an intervention population (Chipulukusu compound), where implementation of the DOTS strategy is an integral part of the HIV/AIDS home care programme, and in a control population (Twapia compound) with district TB services but as yet without coverage by the HIV/AIDS home	Community-based DOT combined with HIV/AIDS program.

	care programme	
2003(Colvin M 2003)	Assess the acceptability and effectiveness of traditional healers as supervisors of TB treatment in an existing directly observed treatment (DOTS)	The treatment outcomes were not given in the report
2003(Nyirenda TE, Harries A.D et al. 2003)	Evaluate the impact on the Lilongwe district tuberculosis programme performance of decentralisation of TB services, including extending the range of options for supervision of DOT during the initial phase of treatment	-Compared the treatment success between hospitalization DOT and other options - Involved with HIV/AIDS programme
2003(Salaniponi FM, Gausi F et al. 2003)	Determine the site of DOT during the initial phase of treatment and the effectiveness of the new regimen	Compared the treatment regimen between 8 months and 6 months of the treatment
2004(Senya S 2004)	Describe the first community-based DOTS contribute to multidrug-resistant TB patients	Qualitative study
2004(Banerjee A 2004)	-Examine traditional healers' (THs) diagnostic and treatment practices for TB - Understand health-seeking behavior for TB amongst tribal groups - Evaluate the acceptability of THs to public health workers - Assess how THs can collaborate with the TB programme	Qualitative study
2004(Kironde S and S 2004)	Describe and evaluate the involvement of the two TB	The main outcome was not the treatment success

	oriented NGOs working in the Northern Cape province	
2005(Escott S 2005)	Document the experience of people involved in the community-based TB	Qualitative study
2007(Okanurak K., Kitayaporn D. et al. 2007)	To investigate patterns of drug administration for TB patients and to determine whether these patterns affect treatment success rates	Compared the treatment success between health facility based DOT with family DOT and self-administrated treatment
2008(Egwaga S, Range N et al. 2008)	Assess the burden of the current treatment strategy, and opinions on a proposed new strategy where patients are able to choose the place of treatment and the treatment supervisors, and receive treatment as a daily combination tablet	Qualitative study
2009 (Weiguo Xu, Wei Lu et al. 2009)	To improve treatment outcomes by understanding of particular barriers to patient's adherence	This study was to improve the patient's adherence to TB treatment
2009 (Saidi Egwaga, Abdallah Mkopi et al. 2009)	Compare the treatment outcomes for patients who chosen home-based DOT treatment with those who chosen health facility-based DOT treatment	The majority of DOT supervisors in the intervention were family members (76%)
2010(Sanneh AFNS and JI 2010)	Compare the TB treatment and outcomes before and after the introduction of DOTS medication and the perceptions/attitudes of defaulters in the Western Division of the Gambia	This study was to compare the treatment regimen 3 times per week with daily treatment in the health clinics. It wasn't compared the DOT approaches between CDOT and HC-DOT
2011(Akhtar S., Rozi	Evaluate WHO defined	This study was compared the

S. et al. 2011)	tuberculosis treatment outcomes for patients under directly observed treatment at a health facility or at home DOT in urban Pakistan	treatment outcomes between health facility-DOT with family-based DOT, which the DOT watchers were family members
2012((David K. Mafigiri, Janet W. McGrath et al. 2012)	Examine modified community-based DOTS as “proof of concept” by identifying how the patients’ social support system may contribute to treatment seeking through task shifting in a high prevalence urban setting of Kampala, Uganda	Qualitative study

Appendix 4: Topic guide for the qualitative study

<p>Patient</p>	<ul style="list-style-type: none"> - How did you know that you had TB? - What procedures did you take before starting the treatment? - For what type of DOT are you treated? - How did you select this treatment? - Who was your DOT watcher? - Where did you swallow medicines? - How often did you go to take medicines with your DOT watcher? - Did you have any problem during the treatment? - Have you ever given anything (money, presents) to your DOT watcher? - What do you like about DOT system (or TB treatment) in your HC? - What do you dislike about DOT system in your HC? - If you will be treated with TB again, would you be happy to be treated with the same type of DOT? - Do you have any suggestions or recommendations to improve the DOT system in your HC?
<p>DOT watcher</p>	<ul style="list-style-type: none"> - What do you do for living? - What is your education level? - Why were you selected as a DOT watcher? - Did you receive any training before started this job?

	<ul style="list-style-type: none"> - What are your responsibilities as a DOT watcher? - Where did you see patients taking medicines? - How often did you see patients? -What do you do if a patient missed taken medicines? - What problems do you face since you worked as DOT watcher? - Are you paid for this job? - What work related difficulties have you encountered? - What do you like about implementing CDOT or HC-DOT in your village? - What do you dislike about implementing CDOT or HC-DOT in your village? - What would you recommend to improve CDOT or TB treatment in your HC? - What do you think about the view of people in your village regarding the CDOT system?
<p>Staff</p>	<ul style="list-style-type: none"> -What is your position in this HC? - How long do you work in this HC? - What is you education level? - What are your responsibilities in TB section? - What do you do if you see a patient suspected with TB? - What procedures does patient need to take for TB treatment? - What types of DOT are implemented in this HC? - Do patients have a choice where they want to be treated? - Who is the DOT watcher in this HC?

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| | <ul style="list-style-type: none">- How often do patients need to go to see DOT watcher?- What happens if patient miss the treatment?- Do you have any TB health promotion in the community?- What work related difficulties have you encountered?- What do you think are the strengths of DOT in your HC?- What do you think are the weaknesses of DOT in your HC?- What would you recommend to improve DOT or TB treatment in your HC?- What do you think of the CDOT approached? |
|--|--|

Appendix 5: Sample size calculation

Sample size estimate for cluster randomization design comparison of two proportion

$$N = \frac{(Z_{\alpha/2} + Z_{\beta})^2 [P_1(1 - P_1) + P_2(1 - P_2)]}{(P_1 - P_2)^2} [1 + (m - 1)\rho]$$

where:

N = required sample size

$Z_{\alpha/2} = 1.96$: the z-score for alpha error, corresponding to the probability with which it is desired to be able to conclude that an observed change of size $(P_2 - P_1)$ would not have occurred by chance;

$Z_{\beta} = 0.84$: the z-score for beta error, corresponding to the degree of confidence with which it

is desired to be certain of detecting a change of size $(P_2 - P_1)$, if one actually occurred.

$P_1 = 0.90$: the estimated proportion at the time of the first survey

$P_2 = 0.945$: the proportion at some future date such that the quantity

$(P_2 - P_1)$ is the size of the magnitude of change it is desired to be able to detect

$1 + (m - 1)\rho = 0.60$: design effect which m is number of patients per cluster; m=50 patients per two year

$\rho = 0.017$: Intra-cluster correlation

$$N = \frac{7.84(0.09 + 0.047)}{0.0025}$$

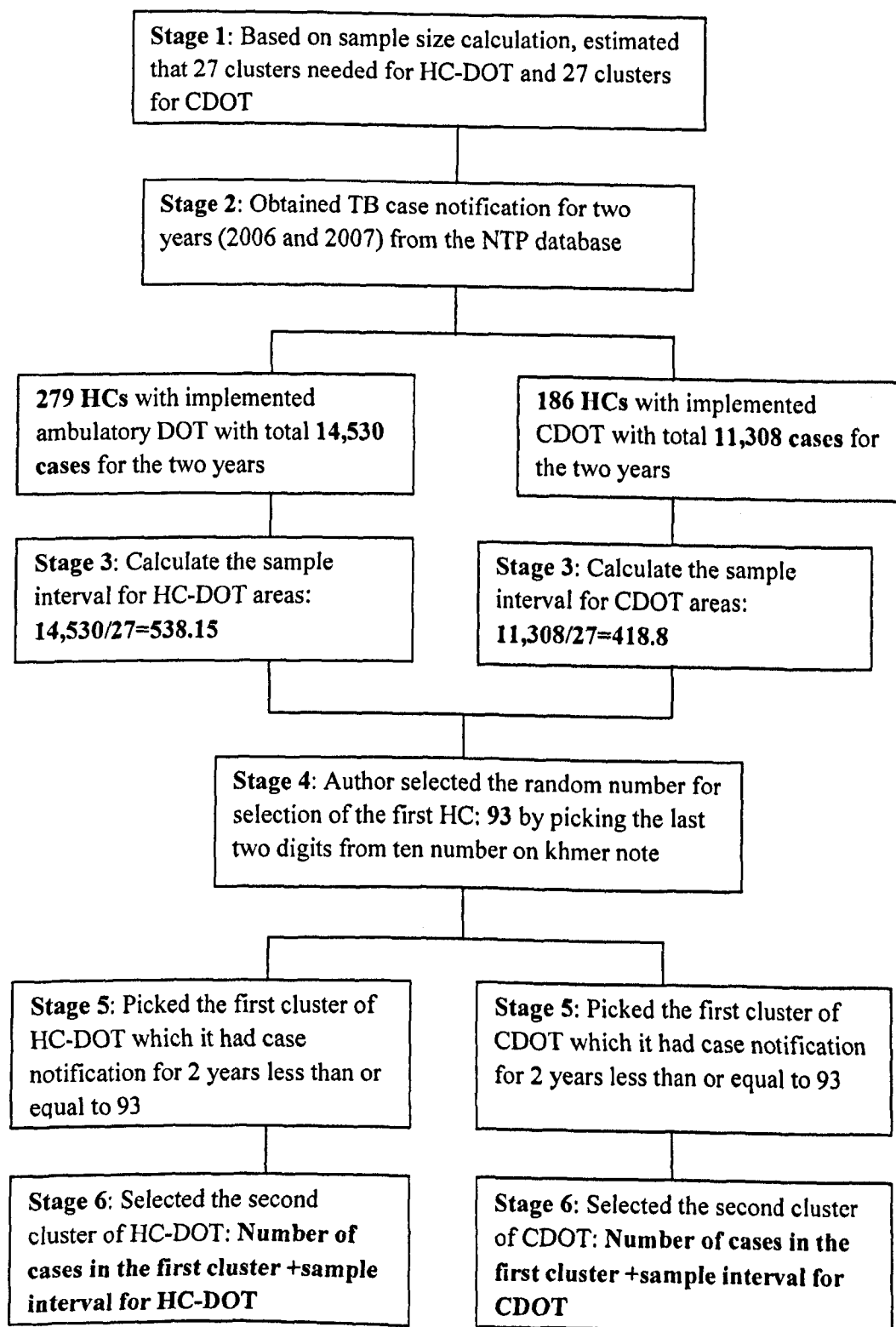
$$0.0025$$

N= 605 patients per each group

N after 10% missing value =665 patients per group

N=665/25; N=27 HCs per group

Appendix 6: Flowchart showing flow of selection clusters of HCs in the study



- We continued with the same method until we got the total 27 clusters of HC for each group

Appendix 7: The list of provinces and health centers selected in the study

Domain	Name of provinces	Name of HCs
Intervention area (CDOT)	Battambang	Odambang I
		Peam Ek
		Bansay treng
		Prey Kpous
		Anloun Run
		Knach Romeas
		Kdol Ta Hen
		Bavel II
	Siem Reap	Kan dek
		Prey Chrouk
		Anloun Samnor
	Kampong Chhang	Svay Chuk
		Kraing Lovear
		Lung Vek
Intervention area (CDOT)	Kampong Cham	Tum Nup
		Skun
		Daun Dom
		Pring Chrum
		Chong Cheach

Intervention area (CDOT)	Kampong Cham	Trapaing Pring
		Chan Moul
		Rum Chek
		Choam Treak
		Thmor Totung
	Kampong Speu	Toul Sala Svay Chochep
		Preahnipean
		Kat Phluk Pheakdey
		Srang
		Phong
	Kampot	Prey Vihear
	Takeo	Cham Pey
		Khvau
		Thlok
		Sra Nge
		Rokar Krau
		Kan Deung
		Kraing Leav
		Roveang
		Tonle Bati
Banteay Mean Chey	Sras Reang	
	Kok Balaing	
	Cham Norm	
	Seur	

	Pursat	Koh Chum
		Wat Luong
	Kratie	Kantout
		Chroy Ban Teay
		Ksim
	No-intervention area (ambulatory DOT)	Phnom Penh
Battambang		Tasanh
		Treng
Siem Reap		Damdek
Kampong Chhang		Koh Thkov
Kampong Thom		Choeung Doeung
		Balaing
		La ork
Kampong Cham		Moha Knohoung
		Chrey Vean
		Svay Teap
		Chey Yo
		Chamkar Andong
Prey Veng		Cheach
		Preak Neak Loeung
		Sdao Kaung
		Pnov
		Rokar
		Cheang Dek

No-intervention area (ambulatory DOT)	Prey Veng	Pratheath
		Kansom Ok
		Svay Antor
		Popes
		Prey Kandeang
	Kampong Speu	Dom Kvet
	Sihanouk Ville	Krong Preah Sihanouk
	Kandal	Kampong Chamlang
		Phnom Bath
		Kampong Phnom
		Prek Tunloab
		Chruoy Takao
		Damnak Ampil
		Kraing Yov

Appendix 8: The information on TB patient for quantitative study

ID Code#, date of data collection: DD/...../MM.....2008

១. ខេត្ត (Province) :.....

២. ស្រុកប្រតិបត្តិ (OD) :

៣. មណ្ឌលសុខភាព (Health center) :.....

៤. លេខសៀវភៅកត់ត្រាមណ្ឌលសុខភាព (HC Register#) :.....

៥. ឈ្មោះអ្នកជំងឺ (Patient's name) :.....

៦. ភេទ (Sex) : 1. ប្រុស (Male) 2. ស្រី (Female)

៧. អាយុ (Age) :.....

៨. អាសយដ្ឋានអ្នកជំងឺ (Patient's address):

លេខផ្ទះ.....ភូមិ.....ឃុំ..... ស្រុក.....ខេត្ត.....

៩. ថ្ងៃ ខែចាប់ផ្តើមព្យាបាល (Date of start treatment):

1. ថ្ងៃDD...../ ខែ MM...../ 2002

2. ថ្ងៃDD...../ ខែ MM...../ 2003

3. ថ្ងៃDD...../ ខែ MM...../ 2006

4. ថ្ងៃDD...../ ខែ MM...../ 2007

១០. លក្ខណៈជំងឺ (TB Type):

- 1. ជំងឺរបេងស្មុតវិជ្ជមានបេកា (BK+)
- 2. ជំងឺរបេងស្មុតអវិជ្ជមានបេកា (BK-)
- 3. ជំងឺរបេងក្រៅស្មុត (EP)

១១. ប្រភេទជំងឺចុះបញ្ជីព្យាបាល (Type of patients):

- 1. ថ្មី (New)
- 2. លាប (Relapse)
- 3. បញ្ជូនចូល (Transferred-in)
- 4. ព្យាបាលក្រោយលះបង់ (Defaulter)
- 5. បរាជ័យ (Failure)
- 6. ផ្សេងៗ (Other)
- 7. ពហុស៊ាំថ្នាំរបេង (MDR)

១២. ករណីសង្ស័យបញ្ជូនដោយ (TB Suspect referred by) :

- 1. អ្នក សហគមន៍ (DOT watcher in community)
- 2. ខ្លួនឯង (Self)
- 3. បុគ្គលិកមណ្ឌលសុខភាព (HC staff)
- 4. ផ្សេងៗ សូមបញ្ជាក់ (Other, please specify) :.....

១៣. ប្រភេទដុតស័ (Type of DOT) :

- 1. សំរាកពេទ្យ (Hospital DOT)
- 2. ដុតស័ចល័ត (Ambulatory DOT)
- 3. តាមផ្ទះ (DOT at Home)
- 4. ដុតស័សហគមន៍ (C-DOTS)
- 5. មិនដុតស័ (no DOT)

១៤. អ្នកឃ្នាំមើលការលេបថ្នាំរបេង (DOT watcher):

1. បុគ្គលិកមណ្ឌលសុខភាព (HC staff)

2. អ្នកស្ម័គ្រចិត្ត (VHSG)

3. អ្នកជិតខាង (neighbor)

4. គ្រួសារអ្នកជំងឺ (patient' family)

5. ផ្សេងៗ- សូមបញ្ជាក់ (Other, please specify)

១៥. លទ្ធផលនៃការព្យាបាល (Treatment outcomes):

1. ជាសះស្បើយ (Cured)

2. បញ្ចប់ការព្យាបាល (Completed)

3. ស្លាប់ (Died)

4. បោះបង់ (Defaulter)

5. បរាជ័យ (Failure)

6. បញ្ជូនចេញក្រៅ (Transferred-out)

១៦. កំណត់ហេតុ រឺ ការសង្កេតក្នុងពេលប្រមូលទិន្នន័យ (Note/observation during the data

collection):

.....

ប្រមូលទិន្នន័យដោយ (Collected by):..... ត្រួតពិនិត្យដោយ (Supervised by):.....

ហត្ថលេខា / ថ្ងៃ (Signature/date).....

ហត្ថលេខា (Signature/date) / ថ្ងៃ.....

Appendix 9: Check list on TB case-finding

1. ឈ្មោះមណ្ឌលសុខភាព (H.C name).....

2. ចំនួនប្រជាជនគ្របដណ្តប់ក្នុងតំបន់មណ្ឌលសុខភាពនេះ (Population).....

3. ចំនួនអ្នកជំងឺរបេងដែលបានស្រាវជ្រាវរកនៅក្នុងមណ្ឌលសុខភាពនេះ (TB case-finding)

Year	BK+	BK-	EP	TOTAL
2002				
2003				
2004				
2005				
2006				
2007				
2008				

Appendix 10: In-depth interview guide for staff

I understand that you are a staff at this HC and have been working for TB section; especially you have a lot of experiences in TB treatment. In my project, I would like to find out what were your experiences in doing this job, and to explore the strengths and weaknesses of implementing DOT as well as CDOT system in your HC. I would like to ask you some questions regarding the TB implementation in this HC. You have right to not answer any questions which you do not feel comfortable. If you don't understand any questions please let me know, I will explain you more; and if you want to stop during the interview, please let me know then we can continue when you feel comfortable to continue the interview. If you are agree to participate in this interview, please sign the consent form then we can continue the interview.

I Back ground information

1. What is your name?
2. What is your current position in this HC?
 - Prompt: What degree qualification in medical field do you hold?
 - Prompt: Could you tell me about your works and job descriptions in TB section?
 - Prompt: How many people work in TB section with you?

II Information about DOT treatment

1. Could you tell me about the TB treatment in your HC?
 - Prompt: What do you do when suspect patient come to see you?
 - Prompt: Where does the sputum test need to be done?
 - Prompt: In average how many days when the sputum results return to the HC?
 - Prompt: What do you do when the test confirm patient having TB?
2. What kinds of DOT treatment implement in your HC?
 - Prompt: Where do patients take medicines during the whole treatment?
 - Prompt: Do patients have a choice to choose their own treatment?

A: For staff at HC-DOT

1. Could you tell me why patients need to take medicines with staff at the HC?

Prompt: Does it apply to all patients?

Prompt: Who are the exceptional cases? What kinds of criteria that applied to those cases?

2. For patients take medicines at the HC, how often do they need to come to the HC?

Prompt: What happens during the weekend or national holiday?

Prompt: What happens if patients miss their treatment?

Prompt: What do you do if you are busy?

3. How long do patients require to come to take medicines at the HC?

Prompt: What happens after the requirement?

Prompt: Do you give them a choice that where they want to treat after it?

Prompt: How do you follow-up with them?

4. For those are exceptional cases, where do patients take medicines?

Prompt: How do you manage with those patients?

Prompt: How do you select their DOT watchers?

Prompt: How often do you see them?

5. Could you tell me what do you or other staff do every time patients come to take medicines at the HC?

Prompt: Do you need to appoint one staff for one individual patient?

6. How do patients know they are completely cured?

Prompt: Do the sputum tests require for all patients?

Prompt: How do patients know when they need to come for the sputum control?

Prompt: What happens when patients do not come for the sputum test?

7. I would like to ask you about the TB program in your HC. Do you have any TB health promotion programs in communities cover by your HC?

Prompt: What are those programs?

Prompt: Who does support those programs?

B: For staff at CDOT

1. What kinds of DOT implement in your HC?

Prompt: What kinds of criteria for patients selected to be CDOT and patients selected to be HC-DOT?

Prompt: Do patients have a choice to select where they want to treat?

2. For patients treat with HC-DOT, where do they need to take medicines?

Prompt: Who is their DOT watcher?

Prompt: How often do they need to come to the HC?

Prompt: What do you or other staff do during they come to take medicines with you?

Prompt: What happens during the weekend or national holiday? Where do they take medicine?

Prompt: What do you do if you are busy?

Prompt: How long do patients need to come to take medicines at the HC?

Prompt: What happens after it?

Prompt: What happens when patients miss their treatment?

3. For patients treat with CDOT, where do they take medicines?

Prompt: Who is their DOT watcher?

Prompt: Do patients have the choice to select their own DOT watcher?

Prompt: How do you arrange for CDOT patients such as arrangement to collect medicines?

Prompt: How often do you need to see them?

Prompt: Why do you need to see them?

Prompt: How do you follow-up with them?

8. How do patients know they are completely cured?

Prompt: Do the sputum tests require for all patients?

Prompt: How do patients know when they need to do the sputum control?

Prompt: What happens when patients do not come for the sputum test?

4. I would like to ask you about the TB program in your HC. Do you have any TB health promotion programs in communities cover by your HC?

Prompt: What are those programs?

Prompt: Who does support those programs?

DOT watcher

1. Now I would like to ask you about the DOT watcher in your HC. How do you select people to be a DOT watcher?

Prompt: What kinds of training do you provide them?

Prompt: What are their responsibilities in TB treatment?

2. How do you organize DOT watchers and patients such as how many patients supervise per one DOT watcher?

Prompt: How do you follow-up their works?

Prompt: What would you do if they have any problems during their works?

3. Who does support the CDOT program in your HC?

Prompt: What kinds of support?

III Incentives

Patients

1. In your HC, do patients need to pay for the TB treatment?

2. Do TB patients in your HC receive any support during the treatment?

Prompt: What are those supports?

Prompt: Does it apply to all TB patients?

Staff

1. Do you receive any incentives during your work in TB and DOT treatment in your HC?

Prompt: Who provides this support?

DOT watcher

1. Does DOT watcher receive any incentive during their works?

Prompt: What types of incentive?

Prompt: Who provides these supports?

IV Strengths and weaknesses of DOT

From this question, I would like to ask you about your experiences and your ideas for implementing DOT in your HC that you have been faced during your works.

1. How do you feel about your works as TB staff in this HC?
2. Since you have a lot experiences in this HC relating to TB and DOT treatment, what difficulties have you faced?

Prompt: How do you deal with various difficulties that you mentioned?

3. What do you think the key factors or reasons for successful implementation of DOT program at your HC?

Prompt: Has the health centre archived its targets in the implementation of DOT program?

4. What would you recommend to improve the DOT or TB program in your HC?

V Perception of implementing CDOT and HC-DOT

A HC-staff

1. Have you ever heard about CDOT program?

Prompt: What do you think about this program?

2. In your opinion, how do you think the difference between CDOT and HC-DOT?

Prompt: Would you implement this program in your HC in the future?

3. Is there anything else would you like to add?

B CDOT staff

1. I understand that your HC implement both for CDOT and HC-DOT, what do you think about these two programs in term of their structures and their differences?

2. In your opinion, between these two programs which one is easier to manage?
Prompt: Why?
Prompt: Which one is produced better results?
Prompt: Why?

3. Is there anything else would you like to add?

Appendix 11: In-depth interview guide for DOT watcher

I understand that you have assigned to be a treatment supporter (or DOT watcher) for TB treatment. In my project, I would like to find out what were your experiences in doing this job, and to explore the strengths and weaknesses of implementing CDOT as well as DOT system in your HC. I would like to ask you some questions regarding the TB implementation in this HC. You have right to not answer any questions which you do not feel comfortable. If you don't understand any questions please let me know, I will explain you more; and if you want to stop during the interview, please let me know then we can continue when you feel comfortable to continue the interview. If you are agree to participate in this interview, please sign the consent form then we can continue the interview.

I Background information

1. What is your name?
Prompt: Are you married?
Prompt: Do they live with you?

2. What do you do for living?

II Information about CDOT

1. I learned that you are selected to be a DOT watcher in your village, what it is like to be a DOT watcher?
Prompt: How did you become to be a DOT watcher in the first place?

2. Have you received any training before started this job?
Prompt: How do you feel about those training?

3. Could you tell me about your jobs as a DOT watcher?
Prompt: What are your responsibilities in this job?
Prompt: How your responsibilities with staff at the HC?

4. Could you describe what actions do you usually take after a patient be assigned to you?

Prompt: Who is arranged to collect medicines for patients?

Prompt: What do you do if the patient has a problem?

Prompt: What do you do if patient doesn't come for medicines?

Prompt: What do you do if it runs out medicines?

Prompt: What do you do if you are busy?

5. Could you tell me what do you do every time the patient comes to take medicines with you?

Prompt: Do you have a choice to select patient to supervise?

6. How do you know if patients who you have been supervised are cured?

Prompt: Do patients need to check their sputum?

Prompt: How do you arrange the sputum control test?

7. Have you ever provided any support besides watching patient taking medicines?

Prompt: What are those?

8. How do you feel to have a contact with TB patients everyday?

Prompt: How about your wife or your children feel to have a contact with TB patient at your house?

III Incentive

1. Since you involve as a DOT watcher, do you get pay for this job?

Prompt: What do you receive from this job?

Prompt: Who give you this support?

2. What do you think about those incentives?

IV Strengths and weaknesses of implementing CDOT

From this question, I would like to ask you about your experiences and your ideas for implementing DOT, especially CDOT in your village that you have been faced since you have become a DOT watcher.

1. Since you have become a DOT watcher, what are works related difficulty that have encounter?

Prompt: What do you deal with those problems?

Prompt: Do you think those problems have been solved now?

2. What do you like about implementing CDOT in your village?

Prompt: Do you think those points achieved the goals which people in your village want?

3. What do you dislike about implementing CDOT in your village?

4. What would you recommend to improve CDOT or TB treatment in your HC?

IV Perception of implementing CDOT

1. How do you feel to be a DOT watcher?

Prompt: What is your view about this job?

Prompt: What do you like about this job?

2. What are the views of people in your community regarding the CDOT system?

Prompt: What do they like about this implementation?

Prompt: What they don't like about it?

3. Is there anything else you would like to add?

Appendix 12: In-depth interview guide for patient

I understand that you have been treated for TB in the past. In my project, I would like to find out what you think of the TB treatment you have been experienced and how it could be improved. I would like to ask you some questions regarding the TB treatment in this HC. You have right to not answer any questions which you do not feel comfortable. If you don't understand any questions please let me know, I will explain you more; and if you want to stop during the interview, please let me know then we can continue when you feel comfortable to continue the interview. If you are agree to participate in this interview, please sign the consent form then we can continue the interview.

I Background information

1. What is your name?
 Prompt: Are you married?
 Prompt: Do you have any children?
 Prompt: Are they living with you?
2. What do you do for living?
3. Do you remember when did you have the TB treatment?
 Prompt: How long you were on the treatment?
4. Where do you live?
 Prompt: How far from your house to the HC?

II Information about DOT

1. Could you tell me how did you find out about your disease at the first place?
 Prompt: Who referred you to go to the HC?
2. What did staff do when you told them about your symptoms?
 Prompt: What kind of tests you took?

3. What happened after you took the tests?
Prompt: How long did it take to get the results back?
4. When you knew about your disease, how did you feel?
5. What procedures did you need to take for the treatment?
Prompt: Who told you?
6. Where did you have the treatment?
Prompt: Who was your DOT watcher?
Prompt: How did you select this treatment?
Prompt: Did you have a choice to select where you wanted to treat?

For patient treated with HC-DOT

1. Where did you take medicines?
Prompt: Who was your DOT watcher?
Prompt: How long did you take medicines with your DOT watcher?
Prompt: What happened after it?
2. How often did you go to take medicines with your DOT watcher?
Prompt: What happened during the weekend or national holiday?
Prompt: What happened if your DOT watcher was busy?
Prompt: What happened if you were busy?
3. Could you describe what happened every time you went to take medicines with your DOT watcher?
Prompt: Do you know why you have to take medicines with your DOT watcher?
Prompt: How were you received by your DOT watcher?
Prompt: Have your DOT watcher ever asked you for anything during the treatment?
4. Did you have any problems during the treatment?

Prompt: What were those?

Prompt: How did you address those problems?

5. How do you feel after you finished the treatment?

Prompt: How do you know you are cured?

Prompt: Did you have your sputum check before finished the treatment?

6. Can you tell me during the treatment; have you ever received any supports?

Prompt: What were those?

Prompt: who else supported for your treatment besides your DOT watcher?

For patient treated with CDOT

1. Where did you take medicines?

Prompt: Who was your DOT watcher?

Prompt: How did you select your DOT watcher?

2. How long did you take medicines with your DOT watcher?

Prompt: What happened after it?

Prompt: How often did you go to take medicines with your DOT watcher?

Prompt: What happened if you were busy?

Prompt: What happened if your DOT watcher was busy?

3. Could you tell me about the arrangement between you and your DOT watcher including medicines collection from the HC?

Prompt: Who was arranging the place where you needed to take medicines?

Prompt: How far from your house to the place where you took medicines?

Prompt: How did you get there?

4. Could you describe what happened every time you went to take medicines with your DOT watcher?

Prompt: Do you know why you needed to take medicines with your DOT watcher?

Prompt: How were you received by your DOT watcher?

Prompt: Have your DOT watcher ever asked you for anything during the treatment?

5. How did you feel about taking medicines given by a DOT watcher instead of staff at HC?
Prompt: What were those?
Prompt: How did you address those problems?
7. How often did you see staff at the HC?
Prompt: Why did you see them?
8. How do you feel after you finished the treatment?
Prompt: How do you know you are cured?
Prompt: Did you have your sputum check before finished the treatment?
9. Can you tell me during the treatment; have you ever received any supports?
Prompt: What were those?
Prompt: who else supported for your treatment besides your DOT watcher?

III Strengths and weaknesses of implementing CDOT and HC-DOT

1. Are you satisfied with the treatment which you have treated?
Prompt: Why?
2. From your experiences, how do you feel about the treatment that you received?
Prompt: What do you like?
Prompt: What you don't like?
Prompt: What should be improved?

For HC-DOT patient

3. Have you ever heard about CDOT?
Prompt: What do you think about this treatment?
Prompt: What do you think about the view of your village towards CDOT?
Prompt: How do you feel about taking medicines given by someone rather than staff at the HC?

4. In the future if your family member or your friend has to treat with TB, what kind of treatment you would recommend them?
Prompt: Why?

5. Is there anything you would like to add?

Appendix 13: Consent form for participants interview in the study

Informed consent form is for

(Please tick one for applicable participant)

Health Staff

Patient

DOT watcher

This informed Consent Form has two parts:

1. Informed Sheet (to share information about the study with you)
2. Certificate of Consent (for signature if you agree that you may participate)

You will be given a copy of the full Informed Consent Form

Part I. Information sheet

You understand that you are being asked to take part in a research conducted by The London School of Hygiene and Tropical Medicine and the National Tuberculosis Control Program. Your participation is voluntary and your employer will not know whether or not you decide to participate so your job will not be affected in any way by participating in the study.

PURPOSE OF THE STUDY

The purpose of this study is to evaluate the structured differences between community and health centre-based DOT, to evaluate the treatment success between these two programme and especially to assess their strengths and weaknesses. The study will ask for your opinion and advice about your treatment experience with these approaches and how we can improve TB treatment with DOT services in this area.

PROCEDURES

If you volunteer to participate in this study, we would like you to participate in an interview. The maximum length of time of your participation in this study will be about 1-1.5 hours. If you so wish, you may withdraw from the study at any time.

You will be interviewed in private where no one else can hear the questions or your answers. We will either use tape recorder to record your answers and also write down your answers. The interview will take place here, at your place of work or at the place that is convenient for you.

POTENTIAL RISKS AND DISCOMFOTS

This study involves the collection of information and your opinions; there may be some discomfort, in responding to questions about disclosure of information and your expression of opinions. If some of the questions are found to be discomforting to you, you can stop any time.

POTENTIAL BENEFITS TO SUBJECTS AND/OR TO SOCIETY

By telling us all about information you know and your shared experiences, we will learn about the advantage and disadvantage of implementing community and health centre-based DOT. As a result, this will help the NTP and the Ministry of Health in Cambodia to develop and improve TB treatment service in your area as well as in the whole country. You will benefit from this program and so does your community.

CONFIDENTIALITY

We will follow the strictest rules of privacy protection to insure your confidentiality. No one will have any way to connect your name with your results from the interviews

PARTICIPATION AND WITHDRAWAL

You can choose whether to be in this study or not. If you volunteer to be in this study, you may withdraw at any time without consequences of any kind. You may also refuse to answer any questions you do not want to answer and still remain in the study.

IDENTIFICATION OF INVESTIGATORS

If you have any questions or concern about the research, please feel free to contact:

Name:.....Researcher, Tel.....

Name:.....Researcher assistance

Tel:.....

Part II. Certificate of consent

I have read the foregoing information, or it has been read to me. I have been satisfactorily informed about this study with its possible risks and benefits. I have had the opportunity to ask questions about it and any questions that I have asked have been answered to my satisfaction. I consent voluntary to participate as a subject in this study and understand that I have the right to withdraw from the study at any time without in any way affecting my further medical care. I understand that I am free to quit at any time, even after signing this form.

Printed name of subject: _____

Signature of subject _____

Date: _____

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