UNIVERSITAS INDONESIA

TREATMENT PLACE IN MDR-TB PATIENTS DURING PRIMARY TB TREATMENT: ITS ROLE ON PATIENT COMPLIANCE AND FREE DRUG PRESCRIPTION

SKRIPSI

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FACULTY OF MEDICINE
INTERNATIONAL CLASS PROGRAM
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A final project report presented to Universitas Indonesia
in partial fulfillment of the requirements for the
Degree of *Sarjana Kedokteran* (Bachelor of Medicine)

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FACULTY OF MEDICINE
INTERNATIONAL CLASS PROGRAM
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MAY 2011

STATEMENT OF ORIGINALITY

This final project (undergraduate) is of my own composition,

any and all outside resources, whether quoted or referenced

have been stated as such.

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Tanggal : 27 Mei 2011

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Research Title	: *TREATMENT PLACE IN MDR-TB PATIENTS DURING PRIMARY TB TREATMENT: ITS ROLE ON PATIENT COMPLIANCE AND FREE DRUG PRESCRIPTION*

has successfully been scrutinized in front of The Board of Examiners and accepted as a prerequisite towards attaining the *Sarjana Kedokteran* (Bachelor of Medicine) degree from the Faculty of Medicine, Universitas Indonesia

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Jakarta, 27 May 2011

The Author

AGREEMENT OF FINAL YEAR PROJECT PUBLICATION FOR ACADEMIC PURPOSES

As an academic member of Universitas Indonesia, I, the undersigned:

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Faculty : Kedokteran

Type of work : Final Project (Undergraduate)

for the further development of science, hereby agree to grant Universitas Indonesia a **Non-Exclusive Royalty-Free Right** to my scientific paper, with the title:

The Role of Treatment Place on Patient Compliance and Free Drug Prescription in MDR-TB Patients during Primary TB Treatment

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I hereby affirm that I have made the above statement truthfully and and it is written under my own volition.

Prepared in : Jakarta

Date : 27 Mei 2011

Signed

(Albert Sedjahtera)

ABSTRAK

Nama : Albert Sedjahtera
Program Studi : Pendidikan Dokter
Judul : Tempat Pengobatan pada Pasien MDR-TB selama Pengobatan TB Pertama: Peran terhadap Kepatuhan Pasien dan Pemberian Obat Gratis

Kemunculan MDR-TB menghambat program pemberantasan TB dan berakibat pada meningkatnya angka kematian dan beban control TB. Tempat pengobatan TB, termasuk riwayat pengobatan, sangat mungkin merupakan predictor MDR-TB yang kuat. Tujuan dari studi ini ada untuk mengidentifikasi dan menganalisis tempat pengobatan TB primer sebagai salah satu factor yang mungkin berkontribusi dalam perkembangan TB menjadi MDR-TB. Pengumpulan data dilaksanakan pada bulan Desember 2009 hingga Agustus 2010. Mengguanakan metode cross-sectional, data didapatkan melaui wawancara mendalam dengan 50 pasien MDR-TB yang sedang mendapatkan pengobatan di klinik MDR-TB RS Persahabatan. Dalam jumlah besar pasien MDR-TB mendapatkan pengobatan di *puskesmas* (38%) dan dokter praktik pribadi (28%). Tidak ditemukan adanya assosiasi antara tempat pengobatan TB pertama dan kepatuhan pasien sedangkan assosiasi terlihat antara tempat pengobatan TB pertama dan peresepan obat gratis.

Kata kunci : TB, MDR-TB, Tempat Pengobatan, Obat Gratis, kepatuhan

ABSTRACT

Name : Albert Sedjahtera
Program of Study : Medicine
Judul : Treatment Place in MDR-TB Patients during Primary TB Treatment: Its Role on Patient Compliance and Free Drug Prescription

The emergence of MDR-TB hampers TB eradication program which resulted in high fatality rate and increase burden of TB control. TB treatment place, including history of treatment, might be a strong predictor of MDR-TB. The purpose of this study is to identify and analyze primary TB treatment place as the contributing factor that may lead to the development of TB towards MDR-TB. The data collection was done from December 2009 to August 2010 at Persahabatan Hospital. Using cross-sectional method, data is obtained through thorough interview of 50 MDR-TB patients undergoing treatment in MDR-TB Clinic in Persahabatan Hospital. Large proportion of MDR-TB patient received their primary TB treatment at *puskesmas* (38%) and private Practice (28%). It is found that there is no association between primary TB treatment place and patient compliance while association appears between primary TB treatment place and free drug prescription.

Keyword : TB, MDR-TB, Treatment Place, Free Drug, Compliance

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CHAPTER 1: INTRODUCTION

1.1 Background

Tuberculosis (TB) is a serious global health problem. Over one third of world population has been infected with M. Tuberculosis, the bacterium responsible to cause the disease. In 2009 alone, the incidence of TB were estimated ranging from 8,9 million – 9,9 million. The cases distribute among all countries worldwide with the predisposing area in Asia(55%) and Africa (30%).[1] Moreover, TB causes a devastating effect in causing mortality as it included in ten leading causes of death in low and middle-income countries[2] with nearly 2 million people died annually[1].

In fact, the curable rate of TB is high, exceeding 95%[3], the treatment success depends highly in the usage of two main first-line drug, isoniazid and rifampicin, both account for the most potent bactericidal and sterilizing drug in the regiments respectively.[4] Resistance to both drugs, termed Multi-Drug Resistance TB (MDR-TB), lead to the usage of second line drugs which have less efficacy and higher toxicity. As a consequence, treatment time will be prolonged (more than 12 month) while failure and fatality rate increased.

The emergence of MDR-TB should not be taken lightly because other major concern could arise. The MDR-TB can develop further resistance to the second line drug to become XDR-TB (Extensively Drug Resistance-TB) with debilitating effect, higher mortality rate and even lower cure rate thus become obstacle to TB control globally.[5]

Every year more than 400,000 cases of multidrug-resistant TB (MDR-TB) emerge as a result of under investments in TB control, poor management of anti-TB drugs and transmission of drug-resistant strains.[6] Moreover, physician error and patient non-compliance are proposed to be the underlying causes in most cases of MDR-TB development.[3]

Directly observed Treatment Short-course (DOTS) strategy, developed in early 1990 by WHO and IUATLD (International Union against TB and Lung Diseases) and recommended by WHO in 1995, has been recognized and proven to be the

most cost-effective strategy in controlling TB. This strategy is also proven to prevent and reduce the emergence of drug resistance.[7, 8] Consequently, World Health Assembly resolution (WHA62.15) includes the enhancement of quality and coverage of DOTS as important measure in preventing the development of MDR-TB.[1]

Since 1995, the National TB control Program (NTP) in Indonesia has adopted DOTS strategy and has already been applied to *puskesmas* (public health centre), integrate to their primary services.[9] Nevertheless, the case of MDR-TB is still remaining high. Indonesia is included among the 27 MDR-TB burden countries, classified based on incidence of more than 4000/year, with estimation of 8900 people contracted from MDR-TB.[1] in which 1.8% are new TB cases and 17% are from retreated TB patients.[10]

This relates to the fact that not all TB patients come to *puskesmas*; significant number of patients also visits other health care provider, which do not fully implement DOTS strategy to the system, such as clinic, hospital, private practitioners and company doctor.[11]

Indeed, strengthening DOTS implementation by NTPs is essential but not enough to meet the global TB control target; To overcome this problem, public-private mix (PPM) approaches is recommended by WHO to engage all health providers in TB care and control.[12]

According to the report of joint external TB Monitoring control Indonesia.[13], MDR-TB is more prevalence in private sector. Some factors are suspected to contribute to the development of resistance TB strains related to the TB treatment place, such as: lack of compliance with international/national treatment guidelines, inadequate drug regimens due to financial constraints, and poor quality of drug in private market.[13] The study is conducted to describe the primary treatment place of MDR-TB patients before they developed drug resistance and find out if there is correlation of treatment place to patient compliance and free drug prescription.

1.2 Identification of Problems

1. Where does MDR-TB patient receive primary treatment of TB?
2. Does primary TB treatment place associate with patient compliance?
3. Does primary TB treatment place associate with free drug prescription?

1.3 Research Scope

The sample of this research is the MDR patients who are getting treatment in Persahabatan Hospital, Jakarta. This pilot project is able to give treatment of MDR-TB cases according to standardized guidelines and ensures the reliable diagnosis of MDR-TB patients.

This project is part of a bigger project by a group that consists of six members. Each group member studies one or more risk factors those may be responsible for the development of MDR-TB from TB. This study only accounts primary TB treatment place, compliance, and free drug as the possible risk factors.

This study investigates the primary TB treatment place, the first place in which the MDR-TB patients received their TB treatment before developed resistance. Moreover, this study also looks into the association of TB treatment place to patient compliance and whether the patients received free drug or not.

1.4 Hypothesis

DOTS strategy has proven to prevent and reduce the emergence of drug resistance.[7,8] However, this strategy is not evenly implemented in all TB treatment place[13]; it is highly implemented only in some places whereas in other places the strategy is poorly implemented.

The expectation of this study is that seeking treatment to the treatment place with low implementation of DOTS strategy is high in MDR-TB patient.

Several studies have confirmed the DOTS strategy effectiveness in enhancing patient compliance.[9, 14, 15] Thereby, this study hypothesizes that:

H_0: Primary TB treatment place does not associate with patient compliance

The linkage of treatment place to DOTS strategy should be related to the free drug prescription.[16] Thereby, this study hypothesizes that:

H_0: Primary TB treatment place does not associate with free drug prescription

1.5 Research Objective

1.4.1 General objective

The general objective of this study is to identify and analyze primary TB treatment place as the contributing factor that may leads to the development of TB towards MDR-TB.

1.4.2 Specific objective

1. To describe the primary TB treatment place of MDR-TB patients
2. To find out whether primary TB treatment place associate with patients compliance
3. To find out whether primary TB treatment place associate with free drug prescription

1.6 Research Benefit

1.5.1 For Researcher

1. To develop an interest in research
2. To gain experience and knowledge in doing research
3. To train and apply effective communication skill within society
4. To gain more knowledge about TB and MDR-TB

1.5.2 For University

1. To hold the principle of "tri dharma perguruan tinggi" while performing the functions of the institution as a means for education, research and community service
2. To contribute to the vision of Faculty of Medicine Universitas Indonesia in 2014 to become a leading medical research faculty in Asia Pasific Region and as the best 80 medical schools

1.5.3 For Clinician

1. To provide data for future clinicians, general practitioners and specialist to be used in daily clinical practice

1.5.4 For Community

1. To provide society with a further knowledge regarding the MDR-TB
2. To provide the society with suggestions about TB treatments

1.5.5 To Government and Policy Makers

1. To provide essential data for government and policy makers to shape the National Tuberculosis Control Program particularly in preventing the emergence of MDR-TB
2. To provide evidence data for government and policy makers to evaluate their program in regard of the National Tuberculosis Control Program

CHAPTER 2: LITERATURE REVIEW

2.1 Tuberculosis

2.1.1 Definition & Etiology of TB

Tuberculosis (TB) is a contagious bacterial disease which most commonly affects lung (pulmonary TB) and less frequently involves other part of the human body (extrapulmonary TB). Lymph nodes, pleura, genitourinary tract, bones and joints are the common site of extrapulmonary infection.[17]

Mycobacterium tuberculosis was first identified by Robert Koch in 1884 as the causative agent of TB. The microbes account to be the etiologic agent in most cases, however, there are other species of mycobacteria (atypical Mycobacteria) which could also cause TB such as; *M.bovis* and *M.africanum.*[18]

The cell wall of Mycobacteria is composed of high content mycolic acids (a characteristic of Acid Fast Bacilli), in which the bacilli are unable to decolorize with acid alcohol after being stained. Moreover, the permeability of Mycobacteria cell membrane is very low as the mycolic acid linked to underlying arabinolactan and peptidoglycan. Consequently, they possess natural resistance against most antibiotics. Lipoarabinomannan is the other important component of the cell wall to survive within macrophage through the interaction with the host cell.[17]**Transmission & Pathogenesis of TB**

M. tuberculosis is transmitted through droplet nuclei from a person with infectious pulmonary tuberculosis which are expelled by mean of air while the infectious person coughing, sneezing, or speaking.[17] The infectiousness of TB is further enhanced with the presence of waxy outer coat allowing the bacteria to survive for long periods of time thus prolong the duration of contact.[18]

Being infected by TB does not mean the person is contracted from the disease; the risk depends mainly to the host endogenous factors, for instance, age and immunological status.[17]

Once the bacteria are inhaled into the lungs, they are phagocytosed by alveolar macrophage, multiplied, and causing lung inflammation. The inflammation attracts neutrophils and macrophages to phagocytes the bacilli preventing them from spreading. The macrophages, however, fail to kill the pathogen through

lysosomal killing as a result they are multiply within the cell. To encounter this problem, macrophages and lymphocytes release interferon to inhibit the replication. Subsequently, the apoptotic infected macrophages activate cytotoxic T cells to produce a cell-mediated hypersensitivity reaction in which forms granulomatous lesion called tubercle. Inside the tubercle, dying tissue ensembles cheese like materials (caseaous necrosis) while the collagenous scar tissue grows around tubercle in order to isolate the bacilli completely.[19]

Isolated *M. tuberculosis* will remain dormant for life unless alteration of immune system occurs or the live bacilli escape into the bronchi causing the disease to be activated. Thus, the reactivation of TB depends highly in one immune system.[17]

2.2 MDR-TB & Mechanism of Resistance

Multi-Drug Resistant Tuberculosis (MDR-TB) is defined as TB strains resistant to the two main first-line drugs, isoniazid and rifampicin with or without resistance to other drug.[6]

The development of resistance from TB to MDR-TB could be achieved by spontaneous mutations, but it is very unlikely to happen as the characteristic of this resistance is unlinked.[20] Isoniazid mutation occurs once every 10^6 replications, while the mutation to rifampicin occurs once every 10^8. Hence, if both drug are used together, the chance of MDR-TB strains to be acquired is only 1 in 10^{14} (10^8 X 10^6) replications.[21]

Genetic factor is one of the potential causes of drug resistance. Patients with HLA-DRB1*13 and HLA-DRB1*14 are found to have a higher risk of developing MDR-TB.[21]

Several factors other than spontaneous mutations and genetic polymorphism have been proposed to predispose the development of MDR-TB. Among all the factors, history of TB treatment is believed to be the most important predictor of the presence of MDR-TB.[21] This could be divided further into the incomplete and inadequate treatments, the quality of the drugs, and patient compliance to the treatments.[21]

2.3 TB Treatment Place

According to National Guideline[22] on TB treatment, several health care providers are indentified in managing TB; *Puskesmas* (public health care), hospital, clinic, and private practice.

In the implementation of National TB Program, every facility within the national health care structure is involved. The district level of *puskesmas* has become the basic unit for TB control in Indonesia. It is then further categorized into three centres; Microscopy health centre (PRM), Satellite health center (PS), and independent health center (PPM).[13] Although patient can go to at any health facility for diagnosis, in Satellite health centers sputum smear should be processed to microscopy health centre regarding the unavailability of laboratory facilities.

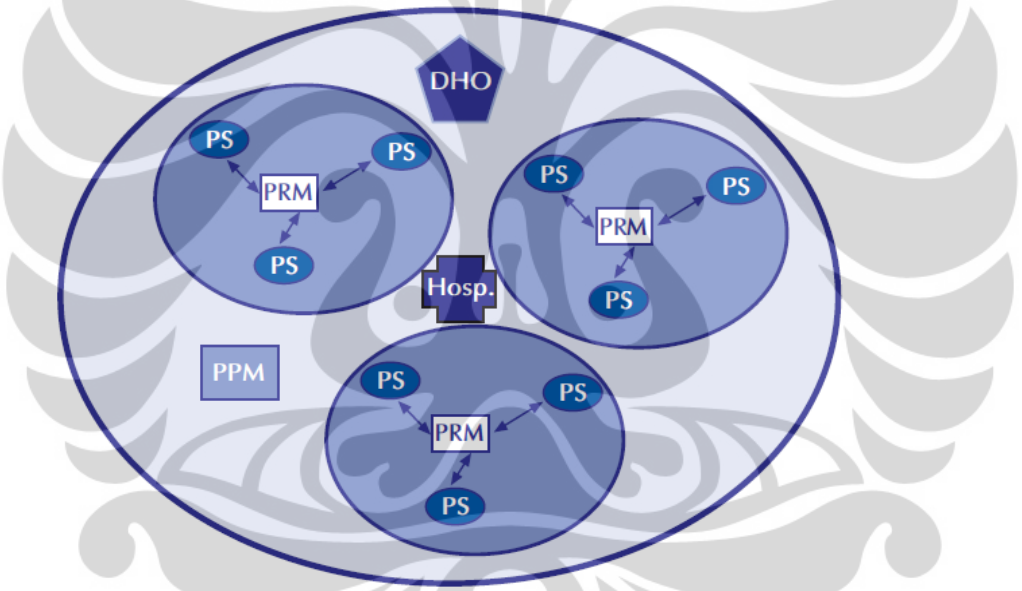


Figure 2. 1 Organization of NTP at district level Error! Bookmark not defined.

Note: PRM=*Puskesmas Rujukan Mikroskopik* (Microscopy Health Centre)
PS=*Puskesmas Satelit* (Satellite Health Centre)
PPM=*Puskesmas Pelaksana Mandiri* (Independent Health Centre)
DHO=Distric Health Office

Puskesmas which is operated by government, under the Directorate of Community services provides the main tuberculosis patient care activities and their service largely are based on NTP guidance.[13] Over 98% of *puskesmas* has implement DOTS strategy to their primary care.[23] Nonetheless, not all TB patients seek

treatment at *puskesmas*, a significant number of people also seek other treatment places[11] where the linkage to the NTP is not fully accessible[13].

DOTS strategy only coves 38% of all hospitals; this number is in fact the average percentage of DOTS coverage in public and private hospitals. In public hospitals, a higher coverage was noticed (59.1%) compares to private hospitals in which only 25.5% have already linked to the strategy.[24] The reason is that public hospitals are managed under the stakeholder in the government, the Directorate of Medical Service. Moreover, private facilities and private practitioners were demonstrated to be the most independent health provider to the NTP.[13]

2.3.1 TB treatment according to National Tb program

According to Indonesia National Guidelines[22], anti-TB drug should be given in the form of combination composed of several types of drug with sufficient number and adequate dosage according to treatment category. Monotherapy anti-TB drug must be avoided while the usage of Fixed Dose Combination (FDC) is highly recommended.

TB treatment should be conveyed in two phases, initial phase and continuation phase.[22] In initial phase, four drugs (rifampicin, isoniazid, pyrazinamid, and ethambuthol) are prescribed to be taken daily with direct observation. While in continuation phase, only rifampicin and isoniazid are given with a longer duration than the initial phase. The purpose of continuation phase is to eradicate the persistent bacteria thus preventing patients from relapse.

In order to ensure the compliance of the patient to take the medication, direct observed of medication ingestion (Direct Observed Therapy-DOT) by treatment supporter is recommended.[25] Health workers are preferred to be the treatment supported, however, if they are not available; family member, community figure, community volunteer or NGO staff could be the a choice of recommendation.[13]

It is an obligation to monitor patient responses toward treatment by mean of sputum check in the end of initial phase, one month before the end of the treatment, and at the end of the treatment.[25] Last but not least, all the data regarding the treatment, bacteriological response and side effect should be recorded and documented.[25]

Monitoring the TB progression is proposed to assess patient response to the treatment, drug side effect and complication. Similar to the treatment, the observation is classified into two phase. In initial phase, clinical assessment should be done at least once in two weeks while microscopic examination is done in the end of the phase and if there is no conversion, the initial phase should be extended for another month and microscopic examination is then performed at the end of the extension phase. Furthermore, if the conversion is still not happened after the extension phase, culture examination and resistance test are needed. Until the result of resistance phase is available, anti-TB drug should keep be given.

In the continuation phase, clinical assessment should be conveyed at least every month. One month before and at the end of the treatment, microscopic examination is performed and if there is no conversion in one of two examinations, the patient is diagnosed as failure where further tests (culture and resistance test) are needed. For patient that fails with category 1, the treatment should change to category 2 whereas patients whom fail with category 2 should be referred to specialist health care place.

Every practitioners involve in TB treatment has responsibilities toward community health. In order to fulfill the responsibilities, the practitioner should not only give anti-TB drug to the patient but also assure the regularity of the treatment until the end. One way to achieve this is by providing information and education to the patients and treatment supporters, which consists of:

- TB etiology and transmission
- Importance of sputum check in follow up
- Importance of regular clinical assessment
- The risk to stop the treatment
- Amount and frequency in drug ingestion
- Drug side effect and measure to overcome the side effect

2.3.2 Free Drug Prescription

To support the availability of free TB drug, the central government by means of Ministry of health endorsed a decree No.1190/Menkes/SK/2004 as one measurement to embrace all of the people including the poor in getting TB medication. The free drug, however, has already been available ever since DOTS strategy implemented in 1994.[16] Additionally, the purpose of providing free drug is to aid DOTS strategy in improving patient compliance.[26]

2.3.3 Engaging other health care provider

As mentioned earlier, NTP program does not cover all the TB treatment place.[13] Thus strengthening the DOTS implementation alone is not enough to meet the global TB control target and prevent the drug resistance.[12] In order to overcome this problem, engagement of other health care providers is needed. Public-private mix (PPM) approach is recommended by WHO to engage all TB care providers and control priority response to MDR and XDR-TB.

Public hospitals have higher linkage to the NTP than the private hospitals. Nonetheless, a study by Probandari[27] found that in the program itself; having access to the NTP, did not ensure the implementation of the program up to their Standard Operating Procedure.

To accelerate DOTS expansion in Indonesia, hospitals and chest clinics must be engaged. Their inclusion is crucial for achieving the national case detection target and preventing the emergence of drug resistance[28]. However, there are several obstacles those could halt the DOTS expansion at the private sector. The obstacles may arise both from the NTP itself and from the private medical sector.

Table 2. 1 Barriers to public-private collaboration in tuberculosis care [29]

Within the national tuberculosis program	Within the private medical sector
Ideological opposition	Inadequate training and lack of information
Lack of information on the private sector	Technical doubts about national tuberculosis programme guidelines
Preoccupation with strengthening and expansion of the national tuberculosis programme	Low priority to public health function: not remunerative
Prejudices about the profit motive and the behavior of private practitioners	Infrastructural limitations to performance of "public health" tasks such as defaulter retrieval
Weak or absent regulatory mechanisms	Doubts about quality of care within the national tuberculosis programme
Absence of precedents; little evidence on replicability	Large unorganized; liaison and interaction challenging

2.4 Patient Compliance to TB treatment

As noted earlier, history of TB treatment is a strong predictor of MDR-TB.[21] There are several factors that correlate with patient compliance to TB medication.

First of all, negligence or incompetence of stakeholder that is responsible in managing the National Tuberculosis Program (NTP) is proposed to be blamed for patient noncompliance to anti-TB medication.[30] This includes lack of medication standardization, inappropriate regiment selection, unavailability of free drugs, and failure in equality of health personnel and absence of treatment program evaluation.

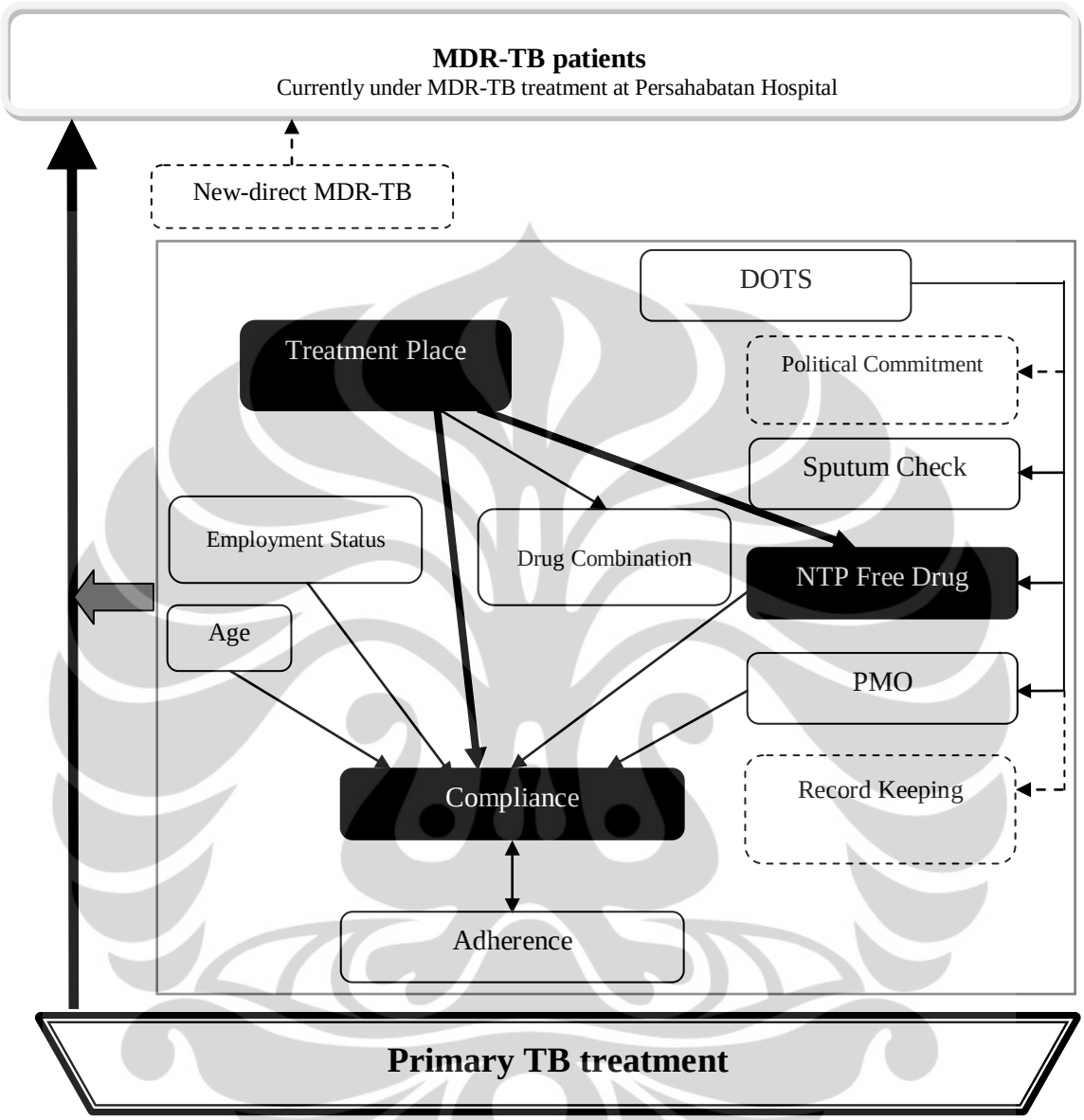
Secondly, noncompliance may result from failure of the one responsible of anti-tuberculosis program at intermediate level.[30] Absence in monitoring drug distribution to central health services, lack of medical prescriptions supervision, absence of any evaluation of treatment and response are seemed to be the caused

Third, the compliance to TB chemotherapy depends on the operation of health services and clinics where patients are exposed directly to the health care personnel.[30] Errors of the central health care personnel such as poor reception condition, insufficient time at the beginning of treatment, absence of procedures

for tracking down patient defaulters, lack of patient monitoring are said to be the technical error and influence patient compliance. Patient compliance are said to be the factor that underestimated by physician.[21]

To overcome the problem of compliance, DOTS strategy by means of direct supervision was recommended to be put into practice. The strategy has become an effective solution to the problem of TB medication non-compliance.[26] DOTS effectiveness in enhancing patient compliance was also confirmed by other studies.[9, 14, 15]

2.5 Conceptual Framework



Note: NTP = National TB Program, PMO = *Pengawas Makan Obat*

Dashed boxes and arrows indicate variables that are not included in this group study

Boxes highlighted in black indicate variables analyzed in this particular study

Boxes highlighted in white indicate variable analyzed by other members of the group

Arrows between the boxes direct independent to dependent variables

CHAPTER 3: DATA & RESEARCH METHODOLOGY

3.1 Study Design

This study is an observational study aimed to investigate the variables at one particular time, thus this study utilizes a cross-section method.

3.2 Time and Place of Study

This study was conducted from December 2009 to May 2011 in Jakarta, Indonesia. The interview is carried out at Persahabatan Hospital (*Rumah Sakit Persahabatan)*, which is located at Jl. Persahabatan Raya No. 1, Pondok Kelapa, East Jakarta. Other process of the study is done at Fakultas Kedokteran Universitas Indonesia, Jl. Salemba Raya 4, Central Jakarta.

3.3 Data Source

This study utilizes primary data aquired from interview with the subjects and secondary data from medical record for confirmation

3.4 Population & Sample

Target population in this study is MDR-TB patients in Indonesia acquiring resistance from susceptible TB. Accessible population in this study is MDR-TB patients undergoing treatment in MDR-TB Clinic in Persahabatan Hospital.

3.5 Sampling Criteria

This study applies some inclusion and exclusion criteria for the subjects.

3.5.1. Inclusion criteria

1. MDR-TB patient who previously received TB treatment
2. MDR-TB patient admitted in MDR-TB treatment at MDR-TB clinic, Pershabatan Hospital.

3.5.2. Exclusion criteria

1. MDR-TB patient who are new-direct cases of MDR TB (Primary MDR-TB)
2. Incomplete data from medical record

3. Patient is not available
4. Patients or patients' family refuse participate in the research

3.6 Data Sampling

The minimal sample size is calculated using the formula to determine the proportion of health problem in the population. Minimum sampling size is calculated as described below.

Minimum Sample Size for Cross-Sectional Study

$$\boldsymbol{n = \frac{\{(Z_1 - \alpha)^2 \times p \times (1-p)\}}{d^2}}$$

where,

n = raw minimum sample size

(Z_1-α) is already determined 1.96 for α=5%

p= prevalence of MDR TB cases developed from TB cases

d= acceptable error of the researcher

In Indonesia, the prevalence of Primary MDR-TB cases is estimated to be in range of 8.1% to 26%. This study utilizes the estimation of prevalence to be 15%, regarding the burden of TB between countries.

$$n = \frac{\{(1.96)^2 \times 15\% \times (1-15\%)\}}{0.1^2}$$

$$n = 48.9804 \approx 49$$

This study utilize convenience sampling methods to obtain the minimum sampling size.

3.7 Variable Identification

In this study, the variable used is nominal variables. This study measures the treatment place seek by MDR-TB patient during their primary TB treatment. The treatment place can be classified according to the linkage to NTP into public

hospital, private hospital, *puskesmas* or primary health center, and private practice/clinic and further be categorized into public and private.

Additionally, this study also intends to find the association of primary treatment place to patient compliance and free drug prescription. Hence, the independent and dependent variable are as below:

Independent variable : - Primary TB treatment place of MDR-TB patient

Dependent variable : - The compliance of MDR-TB patient towards primary TB treatment

- Free drug receive by the MDR-TB patient during primary TB treatment

3.8 Data Analysis Plan

3.8.1. Data Collection

Data collection is done through direct thorough interview with the subjects and confirmation by examining the medical record. The interview is guided by a form that was previously created by the team. The interview is done by six persons, all of whom are the members of the team. This form also includes variables that are used for the research reports of the other members. The complete interview form can be seen in the appendix. The data was collected throughout the period of December 2009 to August 2010.

The data collection is conducted at MDR-TB Clinic, Persahabatan Hospital, Jakarta. A permission letter, dated 24 November 2009, is signed by the Chairwoman of Research Module team for necessary authorization in the hospital.

3.8.2. Data Processing

The results of interviews are written in the form prepared by the interviewer. The data is then converted into table in Microsoft Excel. After that, the data is statistically processed by SPSS 11.5.

3.8.3. Data presentation

The data is presented in graph and table.

3.8.4. Data Analysis

The data is analyzed by statistic method. Descriptive analysis are done for each variable. This study uses chi square to find the association of independent variable to the dependent variable.

3.8.5. Data Interpretation

Data is interpreted to have association from independent towards dependent variables according to the significance of the tests. The null hypothesis is rejected at a *p* value of less than 0.05.

3.8.6. Results Report

The results of this study are written in this report. A presentation is also made in front of supervisor and examiner board.

3.8.7. Research Ethics

An ethic clearance has been filed and approved on 22 November 2009 by Prof. DR. Purwantyastuti, MD, MSc, SpFK.

All of the candidates for subjects would first receive explanation about the background and the objectives of the research by verbal description prior to the interview. If subject agrees to participate in this study, the subject is then required to sign an informed consent.

3.9 Operational Definition

Tuberculosis (TB) is any of the infectious diseases of humans and other animals due to species of Mycobacterium and market by formation of tubercles and caseous necrosis in tissues of any organ. In humans, the lung is the major site of infection and the usual portal through which infection reaches other organs.

Multidrug-resistant TB (MDR-TB) is defined as TB strain that is resistant to at least Isoniazid (INH) and Rifampicin (RIF)

Table 3. 1 Operational Definition

NO	Variable	Definition	Measuring Device	Method of Measurement	Value Measured	Type of Data
1	Primary TB treatment place	The first place a patient received treatment of TB	Questionnaire	Interview	1=Public Hospital 2=*Puskesmas* 3=Private Hospital 4=Private	Nominal
2	Patient compliance	The obedience of the patient to take their medication routinely for the whole primary tuberculosis treatment phase, initial and	Questionnaire	Interview	1=Comply 2=Not comply	Nominal
3	Free drug prescription	The drug received by TB patients without have to pay	Questionnaire	Interview	1=Free 2=Not free	Nominal

CHAPTER 4: RESULT & DISCUSSION

4.1 Primary TB Treatment Place

Various health care facilities are available for TB patients in getting treatment. According to Indonesia Health Survey in 2010[11], a large number of TB patients sought *puskesmas* (39.5%) for their primary treatment place. However, a significant number of TB patients went to other health care provider where the NTP is not fully linked to the system[13], in particular the private practice (19.4%)[11].

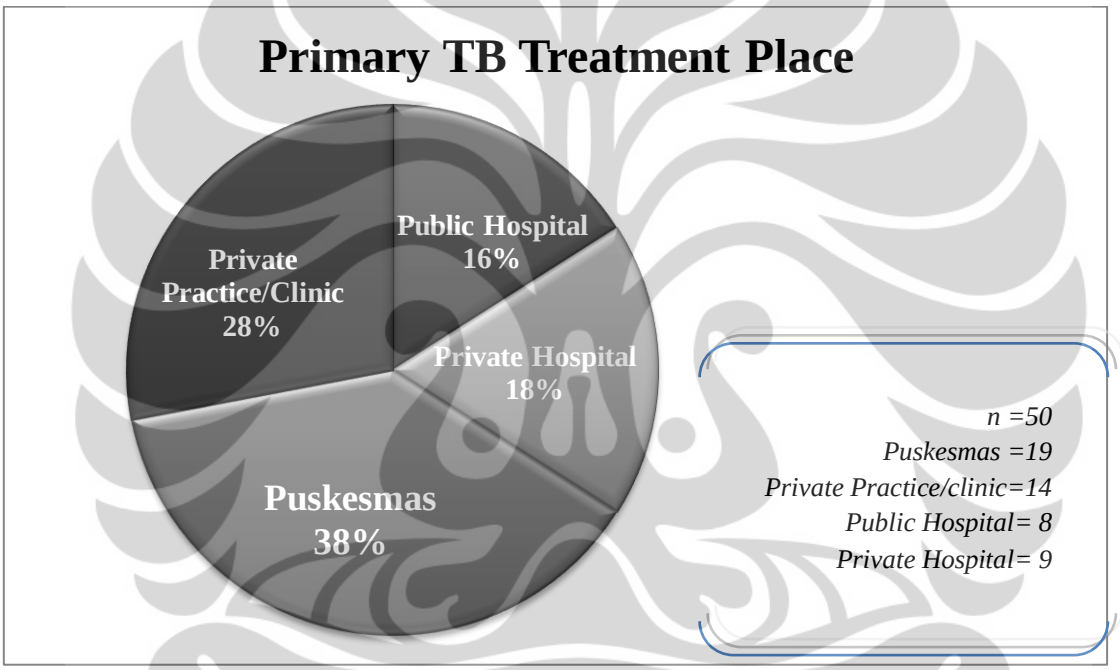


Figure 4. 1 Primary TB Treatment Place

Result of this study (Fig 4.1) shows that most of MDR-TB patients previously received their TB treatment in *Puskesmas* (38%). This finding was totally unexpected knowing that *puskesmas* has the strongest linkage to the NTP (98% DOTS strategy coverage)**Error! Bookmark not defined.** [23] and drug resistance is less likely to develop nder DOTS strategy.[7, 8] Occurrence of MDR-TB indicates low adherence to the guidelines[31, 32], thus it is an embarrassment for our TB control program having possibility that the NTP implementation was malfunction. Moreover, if the area is specified to be the same as this study population area (Jakarta), the risk of developing

MDR-TB seems to be considerably higher in which only 27.7% of all TB patients got treated in *puskesmas*.[11]

Second to *puskesmas,* 28% of all MDR-TB patients in this study got their primary treatment in private practice/clinic before the resistance developed. In this case, getting TB treatment at Private practice possess a higher risk for developing MDR-TB if compared to the seeking pattern of primary TB treatment place based on Indonesia Health Survey in 2010[11] where only 11.5% seek treatment to private practice. This data, however, is not surprising as private practice is said to be completely independent from the NTP.[13, 27] In fact, a guideline[9] based on ISTC for TB treatment which is intended for private practitioners has already been available.

Uplekar[29] mentions that hesitation arises from the managers of National TB to involve private practitioners because they perceive them unmanageable in the absence of regulatory mechanism and they tend to believe only a small percentage of TB patients seek care from private practitioners where the patients, mostly poor people, cannot afford the treatment given. Indeed, the establishment of permanent service linkage to the private practitioners is difficult to achieve as they tend to wander between clinics.[33]

Nonetheless, policy makers, especially in Indonesia, should pay more attention to overcome the obstacle by engaging private practitioners where a significant number of TB patients received TB treatment. If one Look thoroughly at the data, in Jakarta only 28% of patient developed MDR-TB after receiving treatment from private practitioners. One cannot imagine what the number will be on the national population with higher preference to private practitioners in seeking TB treatment (19.4% compare to 11.5%)[11].

In fact, engaging all care providers has become one of the Stop TB Strategy to eliminate TB; this includes the involvement of hospitals both the public and private ones. In Indonesia, hospital engagement in form of Hospital DOTS Linkage project (HDL) started in 2000 with pilot project in Jogjakarta[28] and DOTS coverage to the hospital has reach 38% in 2010[24]. However, a study in Indonesia done by Probandari[27] found that having access to NTP guidelines does not ensure the implementation DOTS to their health services. The combination of both, low coverage and low implementation, seems to be the factors related to the development of MDR-TB in patients who are previously treated in public and private hospital, 16% and 18% respectively.

One of the hindrances for DOTS expansion in developing countries is that the DOTS program itself is not strong enough[29]. Similarly, a study in Jogjakarta by Ahmad[34], found that it is more rational to strengthen the DOTS program than expanding TB control by engaging other provider.

4.2 Patient Compliance

From the interview, it is found that 54% of the MDR-TB patients complied with their primary TB treatment while 46% of the MDR-TB patients are found to be not complied. Patient compliance in this study, by definition, means the patients never skip their medication whether in initial phase or continuation phase. Hence, patients are said to be not comply if they ever skip the medication even once.

This finding alone cannot determine whether patient compliance related to the development of MDR-TB. But if the data is compared to Indonesia health survey 2010[11] which found that 17.3% patients who live in Jakarta do not comply to TB treatment, it is suggested that non-compliance is related to the conversion of TB to MDR-TB. This result supports other studies[3, 4, 21, 31, 35] which propose non-compliance as an important factor that leads susceptible TB to become resistance. The survey[11], however, also includes the patient in ongoing treatment, therefore there is a possibility that the proportion of patient non-compliance is higher.

Moreover, non-compliance level in this study could be higher, regarding the definition of the patient compliance itself where it only defines from whether the patients skip the medication or not. This definition seems to be overly strict as there is broader definition of compliance other than just skip of medication, for instance, higher/lower dose (incorrect dose), timing of medication taken(after or before meal), and treatment duration.[30]

4.3 Association between Primary TB Treatment Place and Patient Compliance

In analyzing the data, Kolmogorov-Smirnov test is used instead of chi-square test because the number of cells with expected count does not fulfill the requirement for chi-square test. The result shows non-significant result ($p>0.05$), meaning that primary TB

treatment place does not associate with patient compliance in previous TB treatment of MDR-TB patient.

In treating TB, besides prescribing drug, practitioners should be able to address poor adherence. One important measure in enhancing patient compliance toward the long duration TB medication is through counseling and education.[25] A study in Nigeria[26] showed that counseling has positive effect to patient compliance. Moreover, Chaulet[30] recommends patient interview session to be at least 20 minutes so that the time is adequate to assess patient knowledge about the disease and the treatment. It is also emphasized in guidelines of TB treatment[9], that health care providers have the responsibility to ensure the patients knowledge about TB.

In this study, the low level of patient compliance could result from not enough knowledge given by all health practitioners regarding the medication. Doctor-patients' ratio in Indonesia seems to be the culprit for this circumstance. At the ratio of 19.9 general practitioners per 100.000 population[36], which is half of the target ratio, there will be an overload of patient that can be managed by the doctor, thus they will probably manage each patient in a limited amount of time and overlooked the importance of education and counseling.

Table 4. 1 Association between Compliance of MDR-TB Patient to Primary TB Treatment Place

Primary TB treatment place	**Compliance**		**Total**
	Yes	No	
Public Hospital	8	0	8
	(100%)	(0%)	(100%)
Private Hospital	5	4	9
	(55.6%)	(44.4%)	(100)
Puskesmas	9	10	19
	(47.4%)	(52.6%)	(100%)
Private practice/Clinic	5	9	14
	(35.7%)	(64.3%)	(100%)

Note: Comparative tests using chi-square test could not fulfill the requirement of expected count, $\chi^2 = 9.044$, df = 1. Kolmogorov-Smirnov 1.084, p>0.05 (not significant)

Subsequently, TB treatment places in this study are further divided into two categories, public and private, in accordance to the linkage of the treatment place to the NTP that is said to be implemented stronger in public sector than in private ones.[13] Public sector consists of *puskesmas* and public hospitals while private hospitals and private practitioners/clinics comprise private group.

From the data analysis using chi-square method (χ^2 = 1.898, df = 1), there is no association between public and private treatment place to the patient compliance ($p>0.05$). This means that being treated in whether Public or Private TB treatment place does not affect patient compliance.

The presence of DOTS strategy in public sector, which is highly linked to the NTP, seems to be an unnecessary stimulus for patient compliance. This finding is in contrary to study by Bello[26] in Nigeria, where DOTS strategy has become an effective solution to the problem of TB medication non-compliance. DOTS effectiveness in enhancing patient compliance was also confirmed by other studies.[9, 14, 15] Thus, it appears that the implementation of DOTS strategy in our study population is not strong enough to affect patient compliance.

4.4 Association between Primary TB Treatment Place and Free Drug

To support the availability of free TB drug, the central government by means of Ministry of health endorses a decree No.1190/Menkes/SK/2004 as one measure to embrace all the people including the poor in getting TB medication. The free drug, however, has already been available ever since DOTS strategy implemented in 1994.[16] Additionally, the purpose of providing free drug is to aid DOTS strategy in improving patient compliance.[26]

This study found that from limited population of 50 MDR-TB patients, 52% patients received free TB drug during their primary TB treatment while 48% patients have to pay for their TB drug.

This finding shows that only 52% of the MDR-TB patients received free TB drug during their primary treatment. It is probably because the patients did not know about the free TB drug program provided by the government. This is related to the low level of knowledge about free TB drug in the community. In accordance to prevalence survey

in 2004, only 19.1% of all TB patient in Indonesia knew that the government provide free TB drug.[37]

In order to compare the significance of primary TB treatment place in determining the free drug given, analysis using chi-square was performed. However, the result of the analysis was not valid as it did not meet the minimum expected count. Consequently, Kolmogorov-Smirnov test was used and the outcome was significant ($p<0.05$). This means primary TB treatment place associate with the free drug given to the MDR-TB patients during their primary TB treatment.

Table 4. 2 Association between Primary TB Treatment Place and Free Drug Prescription

Primary TB treatment place	**Free Drug Prescription**		**Total**
	Yes	No	
Public Hospital	5	3	8
	(62.5%)	(37.5%)	(100%)
Private Hospital	1	8	9
	(11.1%)	(88.9%)	(100%)
Puskesmas	18	1	19
	(47.4%)	(52.6%)	(100%)
Private practice/Clinic	2	12	14
	(35.7%)	(64.3%)	(100%)

Note: Comparative tests using chi-square test could not fulfill the requirement of expected count, $\chi^2 = 28.263$, df = 1. Kolmogorov-Smirnov 1.495, $p<0.05$ (significant)

A higher number of patients received free drug in *puskesmas* compared to in other TB treatment places is not surprising because 98% of *puskesmas* has already linked to the NTP.[23] But there are still patients who did not receive free medication of TB (2%), it possibly because the drug is not available or because his/her own will to take branded drug.

It is also to be expected that a large number of MDR-TB patients did not receive free TB drug during their TB treatment at private hospital and private practitioners since both places have low level of NTP coverage.[13] Thus DOTS strategy is not implemented

well in those facilities and there is no mechanism to receive free drug. Furthermore, if the NTP already linked to the system and patients still have to pay for the drug, the worst possibility would be there is misuse of the free drugs by doctors or other health practitioners by charging fees for drugs supplied freely by the program.[29]

Further analysis divides the health service facilities that give primary treatment according to the link to NTP, into public and private where public consists of *puskesmas* and public hospital where (the control from government is strong for both sectors), while private hospitals and private practitioners were put into one category. The coverage of NTP toward private hospital and private practitioners is lower than that of public hospital and *puskesmas*. Data was analyzed using chi square method (χ^2 = 25.897, df = 1) and association was found between public and private TB treatment place and free drug prescription ($p<0.01$).

Another important issue is about the quality of the free drug itself, where low quality of TB drug is related to drug resistance. This becomes one reason for health practitioners to not trusting the drug provided by the National program because they doubt the quality of the drug, thus unfavorable in giving it to their patients.[29] The quality of the free drug is not only questioned by the practitioners but also by patients. In society there is a stigma regarding cheap drug or free drug which is perceived to have lower quality than that of the branded drug available in the market, they believed that branded drug correlate with better treatment outcome and lessen side effects.[38] Similar finding was reported in a study in Vietnam, where stigma about free drug arose in the society, people believed that free drug was not good in quality that it was something for the poor.[39]

Every health provider should educate all the patients about the knowledge of free drug regardless whether they want the free medication or not. This ensure the transparency that the patients could receive the treatment as well. A good example from India is the existence of prominent boards in the clinics stating that TB drug is free, whereas in Kenya the private practitioners even request patients to sign an agreement clarifying that the patients choose the private care in which they have to pay for TB drug although free drug is available.[29]

4.5 Research Limitation

The sample size of this study would ideally have been larger, but was limited in terms of the few MDR-TB patients available in Persahabatan hospital due to the initiation of MDR-TB treatment pilot project that started recently before the research is conducted.

Cross-sectional method is used in this study. Thus, this study could not elaborate the direct influence of the variable towards development of MDR-TB

Since this study utilizes interview method to obtain data, variability could arise whether from the interviewer or from the patients.

This study did not include the analysis of the year MDR TB patients receive their primary TB treatment and this may result in biased regarding various degree of DOTS coverage in the treatment place.

CHAPTER 5: CONCLUSION & SUGGESTION

5.1 Conclusion

1. Primary TB treatment places which MDR-TB patients underwent treatment before contracting MDR-TB are *puskesmas* (38%), private practice (28%) public hospital (18%) and private hospital (16%).
2. There is no association between primary TB treatment place and patient compliance in previous TB treatment of MDR-TB patients.
3. There is association between primary TB treatment place and free drug prescription in previous TB treatment of MDR-TB patients.

5.2 Suggestion

5.2.1 For Future Study

- Using other type of sampling (i.e probability sampling) to give better representation of the population
- Using case-control study to confirm the association of TB treatment place to patient compliance and free drug given

5.2.2 For Policy Makers

- Strengthen the DOTS implementation in the NTP coverage facilities
- Expand the engagement of other health care provider outside the government health facilities (i.e *puskesmas*)
- Involve all health practitioners to adhere to the guideline and give more education for the patients to enhance compliance
- Promotion concerning the availability and the assured quality of free TB drug

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APPENDIX A: PERMISSION LETTER

UNIVERSITAS INDONESIA
FACULTY OF MEDICINE
INTERNATIONAL CLASS PROGRAM
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Fax. : 62-21-3903004, 3902408 email : international@fk.ui.ac.id

24 November 2009

Nomor : 4640 /PT.02/FK-KI/F/XI/2009
Lampiran :
Perihal : **Permohonan izin penelitian**

Kepada Yth

Ketua Departemen Pulmonologi dan Ilmu Kedokteran Respirasi FKUI

Di RS.Persahabatan
Jakarta

Dengan hormat,

Bersama in kami mengajukan permohonan melakukan penelitian bagi mahasiswa modul Riset FKUI Kelas Internasional (daftar nama terlampir),yang akan melakukan penelitian di Departemen yang Saudara Pimpin mulai dari Desember 2009 - Febeuari 2010.

Sebagai informasi Judul Penelitian Mereka ***Adherence,Compliance,Dosage & Choces of Antimycobacterial Drugs Combination,Age and Referral System n Relation with TB Treatment that Leads to Conversion to MDR-TB***,dengan supervisor Prof.Dr.dr.Purwantyastuti,MSc,Sp.FK dan dr. Erlina Burhan,Sp.P

Besar harapan kami saudara dapat mengijinkan mahasiswa kami, atas perhatian dan kerja samanya kami sampaikan terima kasih.

Ketua Modul Research,

Dr.dr.Saptawati Bardosono,Msc

Tembusan:
1. Arsip

APPENDIX B: ETHICAL CLEARANCE

UNIVERSITAS INDONESIA
FAKULTAS KEDOKTERAN

Jalan Salemba Raya No. 6 Jakarta Pusat
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KAJIAN ETIK
USULAN RISET MAHASISWA MODUL RISET
FAKULTAS KEDOKTERAN UNIVERSITAS INDONESIA

Nama Pengkaji : Prof. Dr. dr. Purwantyastuti SpFK. MSc.
Judul Usulan Riset :
Adherence, Compliance, Dosage & Choices of Antimycobacterial Drug Combination, Age and Referral System in Relation with TB Treatment that Leads to Conversion to MDR TB.
Nama tim peneliti : Albert Sedjahtera, Alberta Jessilya Gunawidi, Anindya Pradipta Susanto, Nicolaas Wahyu Pramono, Mentia Anggeraini, Tissy Fabiola

1. Apakah alasan/motivasi untuk melakukan penelitian ditulis dengan jelas?
   Ya / Tidak
2. Apakah tujuan untuk melakukan penelitian ditulis dengan jelas?
   Ya / Tidak
3. Apakah manfaat dari hasil penelitian ditulis dengan jelas?
   Ya / Tidak
4. Adakah masalah etik yang mungkin akan dihadapi?
   Ada / Tidak
5. Bila penelitian ini menggunakan subyek manusia, apakah penelitian di laboratorium dan/atau percobaan pada hewan harus dilakukan terlebih dahulu?
   Ya / Tidak
6. Bila penelitian ini menggunakan subyek manusia, adakah bahaya potensial yang langsung atau tidak langsung, segera atau kemudian dan cara-cara untuk mencegah atau mengatasi kejadian (termasuk rasa nyeri dan keluhan lain)?
   Ada / Tidak ada
7. Bila penelitian ini menggunakan subyek manusia, adakah dilampirkan contoh surat persetujuan penderita dan rincian informasi yang akan diberikan kepada subyek penelitian)? Ada / Tidak
8. Apakah tim peneliti sudah menjelaskan mengenai penjagaan kerahasiaan data subyek dalam informasi yang diberikan untuk calon subyek penelitiannya? Sudah / Belum

Penelitian ini disetujui / tidak disetujui untuk dilaksanakan, dengan / tanpa perbaikan.

Jakarta, 22/11/09
Tanda tangan Pengkaji Etik:

Prof DR. PURWANTYASTUTI, MD, MSc, SpFK

APPENDIX C: INFORM CONSENT

Formulir Persetujuan untuk Berpartisipasi dalam Riset

Tuberkulosis, atau TB adalah infeksi bakterial yang mnyebabkan lebih banyak kematian di dunia daripada penyakit infeksi lainnya. Hampir 2 milyar orang yang terinfeksi dengan Tuberkulosis di dunia. Tetapi, karena banyak faktor, banyak pasien TB tidak dirawat dengan baik. Hal ini menyebabkan timbulnya MDR-TB atau Multidrug Resistant Tuberculosis. Riset mengenai perubahan dari TB menjadi MDR-TB sedang berkembang pada saat ini.

Anda adalah sample dari riset ini, dan saya memohon kesediaan Anda untuk mengikuti riset ini sebagai partisipan. Setiap data yang diambil akan dijaga kerahasiaannya.

Riset ini adalah bagian dari program pendidikan dokter umum di Fakultas Kedokteran Universits Indonesia.

Terima kasih

Tim Riset MDR-TB

Saya, yang menandatangani formulir ini:

Nama :

Umur :

Telepon:

Telah mendapatkan penjelasan dan mengerti mengenai riset ini, serta menyatakan bahwa saya secara sukarela bersedia unutk mengikuti riset ini dan informasi yang akan diambil dapat digunakan utnuk keperluan riset beserta mengikuti prosedur riset sesuai ketentuan.

Contact person : Albert Sedjahtera 085263574572

APPENDIX D: QUESTIONNAIRE

Particulars

Name	
DOB	
Address	
Contact No.	

Do you know TB can be cured?	Yes No	Adh Comp
How do you know? Who told you?		

First Time Diagnosed TB		
Time/Month-Year (diagnosis or commencement of treatment)		ALL
Attending Physician		
Place Where were you received treatment?	Private Practice, ……. *Puskesmas*, …… Private Hospitals, …… Public Hospitals, ….	REF
Why you choose this place? Who referred you to this place?*	Close to home Close to work place Cheap Trustworthy Referred by previous Other ….	REF
Did you receive free medication from Stop TB program?	Yes No	DRUG REF
Did you find any difficulties to get the drugs	Yes, specify….. No	
Did you know about *PMO*? Who told you about *PMO*?	Yes, who:… No	REF DOTS
Did you feel the presence of		DOTS

PMO is helpful for you?		Comp Adh
Why you choose him/her as *PMO*?		DOTS
Have you ever skipped the medication in initial phase (even once)	Yes No	Comp
Frequency of skip		Comp
Why did you skip the medication	Lazy Forget Side effect Feel well, no more coughs and other symptoms Feel tired, tidak sembuh-sembuh Related to medicine (finish stock, expensive)	Comp
Have you ever skipped the medication in continuation phase (even once)	Yes No	Comp
Frequency of skip		Comp
Why did you skip the medication	Lazy Forget Side effect Feel well, no more coughs and other symptoms Feel tired, tidak sembuh-sembuh Related to medicine (finish stock, expensive)	Comp
Was there sputum check after initial phase	Yes No	ALL

Other Remarks: (eg: drinking habits)

Subsequent Time Diagnosed TB		
Brief History: Time, Place, Medications, DOTS, Adherence, Compliance		
Most Recent Time Diagnosed TB		
Time/Month-Year (diagnosis or commencement of treatment)		ALL
Attending Physician		
Place	Private Practice, ……. *Puskesmas*, …… Private Hospitals, …… Public Hospitals, ….	REF
Why you choose this place? Who referred you to this place?*	Close to home Close to work place Cheap Trustworthy Referred by previous Recommended by others Other ….	REF
Why did you stop to go to previous place?		
Did you receive free medication from Stop TB program?	Yes No	DRUG REF
Did you know about *PMO*? Who told you about *PMO*?	Yes No	REF DOTS
Did you have *PMO*?	Yes No	DOTS
Was your *PMO* the same with previous *PMO*?	Yes No	
Who was your *PMO*?	Name: Core Family (Parents, Spouse, Children) Extended Family Health Officer (*Petugas Puskesmas*, etc.)	DOTS

	Neighbor Friend	
Why you choose him/her as *PMO*?		DOTS
Have you ever skipped the medication in initial phase (even once)	Yes No	Comp
Frequency of skip		Comp
Why did you skip the medication	Lazy Forget Side effect Feel well, no more coughs and other symptoms Feel tired, tidak sembuh-sembuh Related to medicine (finish stock, expensive)	Comp
Have you ever skipped the medication in continuation phase (even once)	Yes No	Comp
Frequency of skip		Comp
Why did you skip the medication	Lazy Forget Side effect Feel well, no more coughs and other symptoms Feel tired, tidak sembuh-sembuh Related to medicine (finish stock, expensive)	Comp
Was there sputum check after initial phase	Yes No	ALL

APPENDIX E: RAW DATA TABULATION

No	Name	Year of Treatment	Primary TB Treatment Place	Compliance	Free Drug
1	NID	2005	*Puskesmas*	Yes	Yes
2	D	2009	*Puskesmas*	No	Yes
3	MY	2005	*Puskesmas*	No	Yes
4	S	2006	Private Practice	No	No
5	J	2005	Private Hospital	No	No
6	S	2004	Private Practice	Yes	No
7	R	2007	Private Hospital	Yes	No
8	R	1997	Private Practice	Yes	No
9	BH	2008	Private Hospital	Yes	No
10	E	2007	Private Hospital	Yes	No
11	S	1990	Private Practice	No	No
12	IH	2002	Public Hospital	Yes	No
13	ES	2007	Private Practice	No	No
14	H	2004	*Puskesmas*	Yes	Yes
15	H	1996	Public Hospital	Yes	Yes
16	A	2006	Public Hospital	Yes	Yes
17	J	2005	Public Hospital	Yes	Yes
18	AS	2002	Public Hospital	Yes	No
19	A	2005	Private Practice	No	Yes
20	M	2008	Public Hospital	Yes	Yes
21	S	2008	*Puskesmas*	No	Yes
22	AY	1997	Private Practice	Yes	No
23	M	1998	Private Practice	No	No
24	A	2009	*Puskesmas*	Yes	Yes
25	M	2002	*Puskesmas*	Yes	Yes
26	F	1990	*Puskesmas*	No	No
27	E	2005	Private Hospital	Yes	No
28	S	2005	Private Hospital	Yes	No
29	AS	2008	*Puskesmas*	Yes	Yes
30	DS	2000	Private Practice	No	No
31	NE	2008	*Puskesmas*	No	Yes
32	S	1999	Private Practice	No	No
33	Z	2000	Private Clinic	No	No
34	R	2006	*Puskesmas*	No	Yes
35	A	2007	Private Clinic	Yes	Yes
36	C	2005	*Puskesmas*	No	Yes
37	DM	2005	*Puskesmas*	Yes	Yes
38	R	1999	Private Hospital	No	No

39	N	2008	Public Hospital	Yes	Yes
40	L	2004	Private Practice	No	No
41	Y	2009	Private Hospital	No	Yes
42	M	2003	Public Hospital	Yes	No
43	S	1990	Private Hospital	No	No
44	Y	2009	*Puskesmas*	No	Yes
45	DHL	2000	*Puskesmas*	Yes	Yes
46	G	2008	*Puskesmas*	Yes	Yes
47	RA	2007	*Puskesmas*	No	Yes
48	J	2004	*Puskesmas*	No	Yes
49	R	2009	*Puskesmas*	Yes	Yes
50	SEW	2006	Private Practice	Yes	No