

CHAPTER III

RESEARCH METHODOLOGY

This chapter presents the methodology applied to investigate the gender differences in delays in initiating tuberculosis treatment under DOTS programme. This chapter addresses the study site, study subjects, size of the sample, sampling procedures, study instruments, measurement of the variables, and methods of data collection, management and analysis. Reliability and validity of study instruments are also addressed.

3.1 Study setting

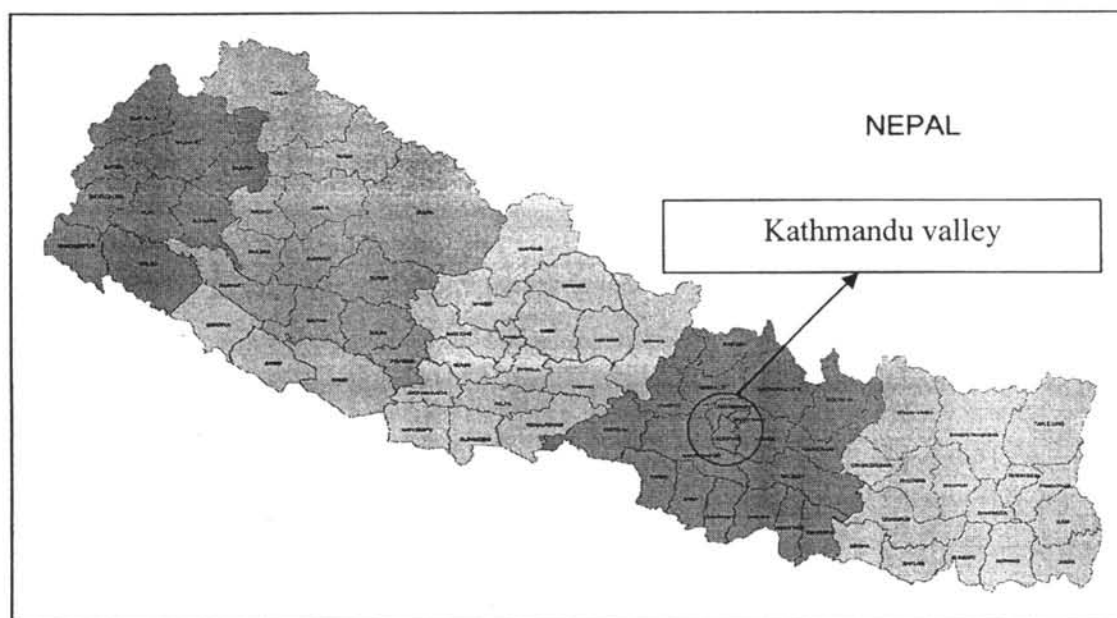


Figure 9: Map shows top three districts (Kathmandu, Lalitpur and Bhaktapur) with high burden of tuberculosis in the Nepal in the year 2003/04.

Tuberculosis is one of major public health problems in Nepal. It has been estimated that the annual risk of tuberculosis infection (ARTI) of Kathmandu valley (4%) is four times higher than hills and mountain (MoH/ NTC, 1994). Kathmandu valley contains 7.2 % of the total national population. About 18% of the national estimated new smear positive cases occurred in these districts in 2004 (NTP, 2004). A large gender gap exists in TB case finding. About 52% of the male estimated TB cases have been detected and enrolled in DOTS, whereas only 32% of the female estimated TB cases were identified in the year 2004. The trend was similar over five years (NTP, 2004). The overall case detection rate was only 42% in the valley which is far below national targets (70%). About 68% of the female cases and about 48% of the male cases are estimated to be undetected in the area. The estimated incidence of new sputum smear positive TB was 200/100,000 population, while the national estimate was 82/100,000. This rate was in males 199.9/100,000 and in females 200.1/100,000 (NTP, 2004). These figures are quite similar to the 22 high burden countries (WHO, 2003a). The notification rate of new sputum smear TB cases was 104/100,000 in males and 63/100,000 in females (NTP, 2004). These findings underscore the large amount of undetected cases, especially in females.

Table 5: Population, estimated new smear positive cases, enrolled cases, and missing cases in the Kathmandu valley-2004.

District	Population		Estimated new positive cases		Enrolled new positive cases		Missing cases	
	M	F	M	F	M	F	M	F
Kathmandu	620403	544821	1241	1090	661	373	580	717
Lalitpur	183041	175477	366	351	167	78	199	273
Bhaktapur	121218	116852	242	234	139	77	103	157
Total	924662	837150	1849	1675	967	528	882	1147

3.2 Research Methodology

Both quantitative and qualitative methodologies were applied in this research. The choice for research methodology was driven by the specific research questions. Both quantitative and qualitative methodologies are tools, and their utility depends on their power to bear upon research questions asked (Kvale, 1996; Starrin et al., 1997). Both approaches were used, based on the hypothesis that both approaches can contribute important insights and ideas regarding subjects' symptom recognition, decision making process, health seeking behavior for TB treatment, choice of health providers, and finally accessing the DOTS services. The nature of qualitative research differs from quantitative research. The term 'quality' refers to what kind, to the essential character of something, while the term 'quantity' refers to how much, how large, the amount of something (Kvale, 1996). Most of the studies in this thesis were based on quantitative research and some issues were addressed using qualitative approach.

3.2.1 Qualitative study

Qualitative research aims to seek a deeper understanding of the social phenomena; studying things in their natural settings; attempting to make sense of, or interpret phenomena in people's meaning. Qualitative research often uses holistic perspectives and more than one data collection method for study, which needs to understand the cultural value and social behavior. If employed appropriately, the method is sensitive enough to capture nuances of the human being (Guba et al., 1994). In this thesis also, qualitative methodology was used to elicit the community's perception about tuberculosis in regard to the local terminology, etiology, symptoms, and choice of treatment and stigma, with emphasis on gender perspective. It was also

considered important to use qualitative methodology in order to help characterize and compare a variety of perceptions and experiences of health seeking behaviors among male and female TB patients, much of which is previously not well known. This design makes it possible to use findings from one focus group discussion to reformulate themes for the next one. Focus group discussion brings the spontaneous generating of questions as they come out naturally from the free-flowing discussion between researcher and respondents, so that the researcher gives attention to guiding the discussion around the study themes.

3.2.2 Quantitative study

3.2.2.1 Analytical study design

The purpose of analytical studies is to test hypothesis about the relationship between health problems and possible risk factors, that is, factors that may affect the probability or severity of disease. The findings of this study help to prevent factors that causes to disease. In this study, the subject of interest is the individual within the population. The object is not to formulate but to test hypotheses. Although individual are evaluated in analytical study, the inference is not to individuals, but to the population from which they are selected. Analytical studies comprise three distinct types of observational studies. They are cross sectional, case-control and cohort studies. In this thesis, cross sectional analytical study design was used.

Cross-sectional studies

Basically this type of study is carried out to identify disease or health related states and suspected determinants as a particular point in time (Enarson et al., 2001). Cross-sectional study is the simplest form of an observational study. It is

based on a single examination of a cross-section of population at one point in time- the result of which can be projected on the whole population provided the sampling has been done correctly.

The aims of this design are to test hypotheses on disease causation by the degree of association between possible determinants and disease, and to assist health service planning by measuring the burden of disease in subgroups and identifying those in greatest need of services. In this thesis hypotheses were tested showing the degree of correlation and relationship between the providers and delays in initiating tuberculosis treatment with DOTS, between gender and delays, between delays to initiating TB treatment and socio-economic factors, between delays to initiating TB treatment and behavioural factors, and between delays to initiating tuberculosis treatment and accessibility factors. Key determinants causing delays to start treatment were identified and possible solutions were recommended to the policy level of the NTP.

Advantages of this design include the following (Enarson et al., 2001):

- Results can be obtained relatively quickly and cheaply
- Large numbers of possible associations can be explored
- Methods of measurement of both determinants and outcomes are standardized

Disadvantages are that (Enarson et al., 2001):

- Temporal relationship between determinants and disease is not always clear
- When disease is rare a large study population is required
- Recall of past events and experiences may be unreliable
- Population being studied comprises survivors of a cohort.

3.2.3 Relationship between qualitative and quantitative methods

It has already been mentioned that qualitative study is very useful to understand the in-depth feelings, ideas, experiences, and thoughts from the open discussion. Qualitative study would be very helpful to understand delay factors in seeking TB care among men and women, decision making process to seek care, choice of the providers and approaching DOTS services. In this study also, the results from the qualitative study were utilized to assess the study's conceptual framework in the real world, and to revise it as appropriate. The qualitative study also helped to construct the questionnaire in a meaningful way, and to avoid leading and sensitive issues in the quantitative study. Basically the quantitative study was used to identify the influencing variables to the study outcomes, with guidance from the qualitative study.

3.3 Study population

New smear positive pulmonary tuberculosis patients enrolled in the DOTS centres, Kathmandu valley of Nepal

3.4 Sample population

3.4.1 Phase I: study population for qualitative study

Four focus group discussions were carried out among the different communities. They were i) Tuberculosis patients; ii) community people with no history of TB; iii) private practitioners and iv) DOTS providers.

3.4.2 Study Phase II: study population for quantitative study

All the registered new smear positive pulmonary tuberculosis patients under 37 randomly selected DOTS centres of the Kathmandu valley between 1st

January and 30th August, 2006 were the sample population. This was matched with the inclusion and exclusion criteria.

3.5 Sample size

3.5.1 Phase I: Sample size for qualitative study

Six to eight participants in each group were selected. Gender balance was respected in selecting process of in each group.

3.5.2 Phase II: Sample size for quantitative study

An extensive literature search is done to understand the prevalence of delay and pattern of delay in TB care seeking. A study carried out in Ethiopia showed that the prevalence of delay more than 30 days was 50% (Demissie et al., 2002). Published articles showed that the mean or median total delay between onset of TB symptoms and initiating of tuberculosis treatment was 8 weeks to 15 weeks. (Olumuyiwa et al., 2004; Long et al., 1999; Sherman et al., 1999; Wandwalo & Morkve, 2000; Lienhardt et al., 2001; Pronyk et al., 2002; Needham et al., 2001). A study carried out in rural area of Nepal in 1999 reported that the mean delay to TB diagnosis was 69 and 99 days in males and females respectively (Yamasaki et al., 2001). The annual report-2004 of the National Tuberculosis Control Programme of Nepal shows that the male and female ratio of case detection of new smear positive cases is about 2:1 (NTP, 2004). These figures were used to calculate minimum sample size using t-test, taking confidence level 95%, and power 80% with male to female ratio 2:1. A total required sample size was calculated at 348 (232 males and 116 females). In fact, we enrolled a considerably larger number of subjects, 616 (379 males and 237 females).

3.6 Inclusion and exclusion criteria

3.6.1 Phase I: Inclusion and exclusion criteria for Qualitative study

- i) Tuberculosis patients: Male and female new smear positive tuberculosis patients currently under DOTS treatment aged between 15 to 50 years old were included.
- ii) Community people with no history of TB: Representatives from mother' group, community volunteers, and social leaders aged between 25 to 60 years old were included.
- iii) Private practitioners: Male and female private practitioners who are currently treating tuberculosis patients were included in the study.
- iv) DOTS providers: Male and female DOTS providers who are currently providing DOTS services at the DOTS centre level were included.

3.6.2 Phase II: Inclusion and exclusion criteria for quantitative study

New smear positive pulmonary tuberculosis patients aged ≥ 15 years were included. Patients who did not like to participate, new smear positive pulmonary tuberculosis patients less than 15 years old, extra pulmonary tuberculosis patients, and re-treatment positive (relapse, failure, and return after defaulter) and smear negative pulmonary TB patients were excluded from the study. It was estimated that about 5% to 10% of eligible TB patients would decline participating in the study.

3.7 Sampling Procedure

3.7.1 Phase I: Sampling procedure for qualitative study

- i) *Tuberculosis patients*: the group consists of 6 to 8 participants, relatively homogeneous with respect to socio-economic status, but not with respect to age. Patients were purposively selected.

- ii) *Community people*: this group was recruited from the representatives of community workers, mother's group, and other lay people in the community by the help of DOTS committee.
- iii) *Private practitioners/pharmacists*: This group consisted of private practitioners who were treating tuberculosis patients at the point of study. The participants of this group were selected with coordination of District Public Health Office of the study area.
- iv) *DOTS providers*: This group consisted of DOTS providers working at the DOTS centre. The members of this group were selected with coordination of District Health Office of the study area.

3.7.2 Phase II: Sampling procedure for quantitative study

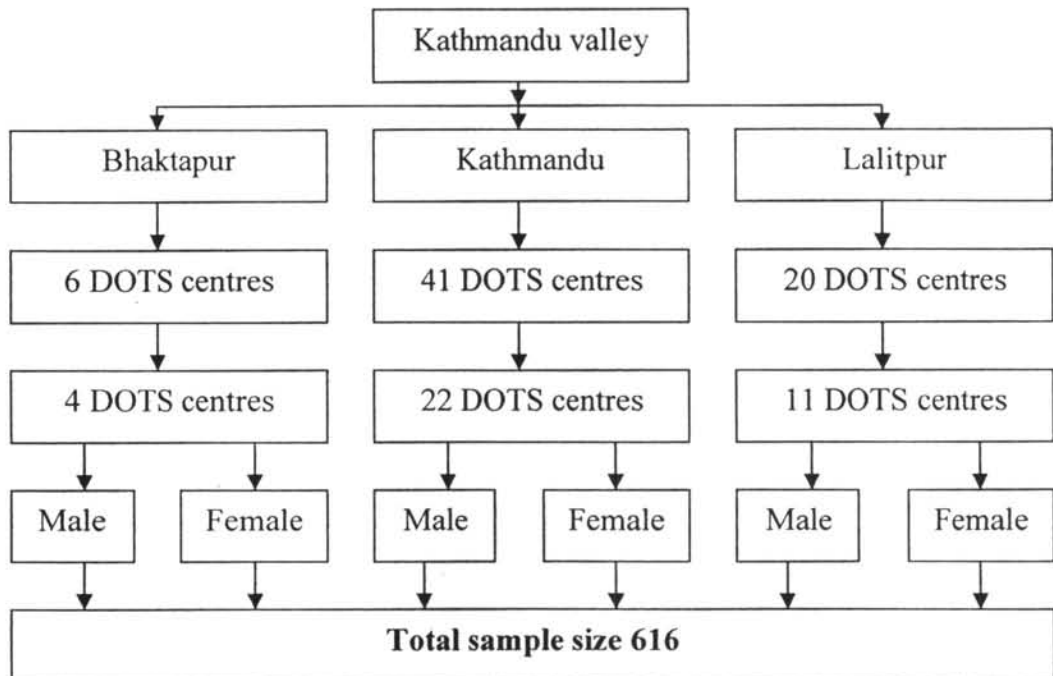


Figure 10: Sampling frame for quantitative study

Steps of sampling

Step 1: Stratification by district; the study area is divided into three districts i.e. Bhaktapur, Kathamndu and Lalitpur.

Step 2: Numbers of DOTS centres were indentified in each district by reviewing TB register and district monitoring sheet as well as the latest annual report of National Tuberculosis Control Programme (2005).

Step 3: At least 50% of the existing DOTS centres in each district were selected by using simple random sampling.

Step 4: Detailed review of the study subjects was done at the DOTS centre. Tuberculosis registered, Tuberculosis Treatment card and TB laboratory register, and referral forms were used for review process. Inclusion and exclusion criteria were matched to every individual of the both sexes.

Step 5: All new smear positive TB patients enrolled between January and August, 2006 were interviewed.

3.8 Data collection instruments

3.8.1 Phase I: data collection instruments for qualitative study

Emergent design in the focus group discussion was used as the data collection tool. Data collection for qualitative study includes group discussion. Guidelines of focus group discussion were developed (annex 1). Some open-ended questions were presented at the beginning and during the discussion.

3.8.2 Phase II: Data collection instruments for quantitative study

A standard structured questionnaire was prepared in English and then it was translated by professional translators into Nepali (annex 2). The questionnaire was composed of 11 parts: the general demographic; socio-economic; recognition of

symptoms and decision making; help seeking behavior; socio-cultural; knowledge about TB; perception about TB; access; behavioral and clinical factors. Patient's expenditure for TB care was also a part of questionnaire. Health system related information was also obtained by using structured questionnaire.

3.9 Validity and Reliability of the instrument

3.9.1 Validity

Questionnaires in this study were developed from the review of published articles and research reports. In addition, information from phase I, qualitative study provided important guidance in developing the questionnaire for phase II, quantitative study. The content validity was assessed from the experts of the Chulalongkorn University and International Union Against Tuberculosis and Lung Disease (IUATLD) Paris, France. Most of the questions in this study were developed regarding health seeking for TB treatment, knowledge, perception, accessibility, socio-economic, stigma and delay measurement from various studies carried out in the different settings around the world (Demissie et al., 2002; Needham et al., 2001; Ngamvithayapong et al., 2003; Yamasaki et al., 2001).

3.9.2 Reliability

The questionnaire was pre-tested for reliability in a non-study district among 32 individuals. Revision of the words and phrases and reordering of the questions were made based on the feedback from the respondents. The whole process of interview was closely monitored to ensure clear understanding of the questions. The history given by the patient was correlated with the date of prescriptions and laboratory test results, to verify the reliability of the patient's account.

3.10 Data collection procedures

3.10.1 Training of the research assistants

Five research assistants were recruited for the study purposes. A two day intensive training was organized for them by the researcher. A standard data collection guideline was used. Emphasis was given on data collection methods, focusing on interview techniques. Field testing was organized and careful attention was given to field procedures. During the training, regarding research ethics and patient's confidentiality, providing the information about the study to the participants and obtaining the informed consents, right of the patients to withdraw from the study at any time were addressed to the research assistants.

3.10.2 Phase I: Focus group discussion (FGD) for qualitative study

The reason for choosing FGDs as the data collection techniques is to utilize properties of group dynamics in order to study the breadth of experience of respondents, thereby gaining maximum variation of answers with adequate depth. The interaction between participants in the groups can provide valuable, sometimes unexpected, information and understanding (Krueger, 1988). FGDs reveal the range of a community's beliefs, ideas, opinions, and attitudes and are valuable for gaining base-line information. The method has limitations in explaining complex beliefs of individuals (for which in-depth interviews are needed) (Krueger, 1988).

The researchers conducted all sessions of FGD with the assistance of a note-taker and a support staff member. The process of organizing each FGD consists in the recruitment of the participants, conducting FGD and analyzing the data. All sessions were recorded with a tape recorder. These focus groups discussion were carried out between November, 2005 and May, 2006.

The main focus of qualitative study was to understand the women's help seeking behavior for tuberculosis especially, in the areas of what do they think about tuberculosis, why don't they give higher priority to their health, what are the socio-cultural factors that contribute to delay in TB care seeking, what is their role in decision making in their households, where do they consult first, how do they present in DOTS centres.

3.10.3 Phase II: Data collection procedures for quantitative study

3.10.3.1 Record review

A standard recording and reporting system is developed and applied by the National Tuberculosis Control Programme of Nepal. All the recording tools; Tuberculosis register, Tuberculosis laboratory register, TB treatment card and Patient card are developed as per the WHO and IUATLD guidelines and applied throughout the country. The details of diagnosis and treatment information of each patient are recorded in these tools. Therefore, diagnosis and treatment information were obtained reviewing TB register, TB Laboratory register, and TB treatment cards.

3.10.3.2 Face to face interview

Interview was carried out at the DOTS centre by using a structured questionnaire. All new smear positive pulmonary tuberculosis patients who were enrolled for DOTS treatment between January 1 and August 31, 2006, were interviewed by trained research assistants. Nearly all patients were interviewed within a month after initiation of anti-TB treatment at DOTS centre.

3.11 Measurement

3.11.1 Dependent variables

Median delays were used to measure all delay intervals i.e. patient delay, health system diagnosis delay, total diagnosis delay, and total delay.

3.11.2 Independent variables

- Socio-demographic factors: type of setting of residence, marital status, and migration status, sex was treated as categorical variables. Median was used to categorize household and children size. Age of the respondents was categorized as per the WHO category.
- Variables in the socio-economic section; educational status, occupation, and main earner in the household were categorized in different levels. Monthly personal income and households' annual income was categorized using median.
- Socio-cultural section: Responses were categorized as yes and no.
- Knowledge: Responses were obtained as correct or incorrect and measured each response accordingly.
- Perception about TB and its treatment: Responses were obtained as agree or disagree. Data were analyzed accordingly.
- Accessibility sub section: Mode of transportation was categorically analyzed. Median was used to characterize the sub-groups for distance to diagnostic, travel cost, traveling and, waiting time.
- Behavioral factors: Variables such as smoking and consumption of alcohol were categorized as yes and no.

3.12 Data analysis

3.12.1 Qualitative data analysis

Modified grounded theory

A modified grounded theory technique (Glaser & Strauss, 1968) for analysis of data was used. The FGDs were tape recorded, transcribed in Nepalese and then it was translated into English. Translation was made by the independent translators in order to maintain the accuracy of the records. Data were analyzed inductively, i.e. raw data were transformed into categories. During the analysis, open codes were applied to segments of the text by the researchers. Constant comparison among open codes was made between men and women. Data were reorganized accordingly and categories were created from the open codes.

The cut and paste technique

The cut and paste technique is a quick and cost effective method for analyzing the transcripts of focus group discussion. Before starting the analysis, the recorded tapes of FGD were transcribed verbatim by the note taker and were verified by the researchers and experts. The recorded information in the tapes was transcribed in handwriting and then the texts were typed into word processor. This method was used because the sophisticated transcribing machines would not be possible to make available in the resource poor settings like Nepal. The researcher carefully read the transcript and identified the sections that would be applicable to the research questions. The researcher classified the major themes and the topic related to each theme. Each theme was coded related to research topics and highlighted by different colors. Each piece of the coded materials was sorted and all materials relevant to a particular topic were collected together for the explanation.

3.12.2 Quantitative analysis

The statistical analysis

Every data form was checked by the researcher. Data validation was done twice; by the research assistants first and then by the researcher. All the data was coded and the codes were verified.

All analyses were conducted using the SPSS statistical package, version 13. Median delays associated with all covariates were calculated separately by gender, and for both genders combined. The specific delays considered were as follows: (1) patient delay; (2) health system diagnosis delay; (3) total diagnosis delay (the sum of (1) and (2)) (Treatment delay was very short, and did not differ by gender. Thus, it was not considered separately in analysis.) The independent variables were divided into the following 12 conceptual blocks: (1) venue/setting (i.e. name of DOTS centre, type of DOTS centre, type of diagnosis centre, district and rural or urban setting); (2) demographic (i.e. age, caste, marital status, household size, number of children); (3) socio-economic (i.e. education, occupation, main income earner, monthly income, and annual household income); (4) symptoms and decision making (i.e. recognition of symptoms, source of recognition of symptoms, decision making for medical help, decision maker, symptoms lead to decision making); (5) socio-cultural (i.e. felt ashamed, hiding TB diagnosis, acquired TB due to sinful act, perceived TB is a heredity disease, isolation, problem with spouse, problem to get married, hesitate to talk, hesitate in mixing, find fault, use of common articles, sleeping place, participate in community events); (6) knowledge about TB (i.e. important symptoms of TB, cause, transmission, curable disease, benefit of DOTS); (7) perception on TB (i.e. coughing, risk of TB, dangerous disease, vulnerable,

jobless, fatal, sinful act); (8) access to TB diagnosis and treatment (i.e. mode of transport, distance, traveling time, travel cost, waiting time, meet health staff, received health education); (9) health-related behaviors (i.e. smoking, drinking, fuel used for cooking, installed chimney in the kitchen); (10) costs incurred between onset of symptoms and TB diagnosis (i.e. direct medical and non-medical costs, lost income, total patient costs); (11) clinical characteristics (HIV status, presence of cough, duration of cough, grading of sputum); and (12) care seeking (i.e. type of provider visited first, providers visited at any time, number of providers visited, was or was not advised to have sputum test).

In bivariate analyses, the Mann-Whitney and Kruskal-Wallis tests were used to compare delay times across different levels of individual independent variables, because these times were not normally distributed. (In chapter IV, results of bivariate analysis are presented only for patient delay and health system diagnosis delay).

In each conceptual block, general linear models (GLMs) were constructed within gender and for both genders combined. Each model included gender and all variables in the block as independent variables. Separate models were constructed for each of the 4 types of delay as dependent variable. These models considered only main effects; interactions were not included. Gender and all other independent variables for which $p \leq 0.10$ in GLMs were considered further. This strategy was used for two reasons, i) to investigate determinants in a manageable, interpretable fashion, and ii) to limit independent variables in any single model, and thus to limit distortion arising from potential co-linearity among large numbers of independent variables.

In the next two analytic steps, multilevel mixed models were constructed for each gender and for all subjects combined (linear mixed model option in SPSS, version 13). First-step models included, as fixed effects, gender and all independent variables for which $p \leq 0.10$ in GLMs. Separate models were constructed for each type of delay as dependent variable. Second-step mixed models included all independent variables for which $p \leq 0.10$ in first-step mixed models. In both steps, to adjust for potential effects of clustering in the data, DOTS center was included as a random factor (covariance structure = variance components).

Results of first-step mixed models are presented in chapter IV as tests of type III fixed effects. Results of second-step (final) models are presented both as tests of type III effects and as regression coefficients, 95% confidence intervals, and p-values. Estimates and p-values of the random covariance parameter DOTS center are also presented. Results are presented for each type of delay; for total delay, only models for males and females combined are presented.

3.13 Ethical consideration

The study was approved by the Ethical Review Committee of Nepal Health Research Council before initiating the field work. In addition, the researcher strictly adhered to the ethical guidelines for researchers, issued by the Nepal Health Research Council. The following general ethical considerations were applied including training for the research assistants regarding research ethics and patient's confidentiality, providing the information about the study to the participants and obtaining the informed consents, all participants were made aware of their right to withdraw from the study at any time, the patient's right not to respond to those questions which they don't wish to respond to as well as the confidentiality of the individual's data and

information. The study participants were identified by clinical records (TB treatment card and tuberculosis register), not by name. These records were available in each DOTS centres.

The participants were assured of confidentiality and the possibility to withdraw at any time. In fact, participants of each FGD expressed considerable interest in taking part in the discussions.

3.14 Biases

The result of the study could be affected due to the recall bias. Due to their long period of time before accessing DOTS services and large scale of shopping for seeking treatment, they might have forgotten some important events such as exact date or interval of beginning of symptoms and first contact to the any type of providers. Therefore, to help with accurate recollection, some additional questions were asked regarding local festival, harvesting time, birth day, wedding ceremony of the relatives or neighbors, or any special events happened in community, during the vacation period of the children and so on to make recall easy of the time of symptoms onset. These attempts would help to minimize the recall biases.

Interviewer bias was reduced by using a structured, standardized questionnaire administered by trained interviewers. Interview guidelines were provided to all the research assistants. There would be little possibility that some respondents might not respond due to not understanding of the question, but interviewers were instructed to follow the guidelines if such situation happened.

Confounding was controlled by using multivariable linear regression and multilevel analysis.

3.15 Scope of the study

Since this study was conducted in the high burden districts of Nepal among new smear positive pulmonary tuberculosis cases (highly infectious), the findings would not be generalized to the whole population of the country due to difficult terrain and multiple ethnic groups with multiple socio-economic situations and cultural value structures.

The patient delay among male and female was calculated as the difference between the duration of first symptom and the time of first consultation. This delay is of major importance; it is the window when people wait while sick, putting off a visit/consult for whatever reason. If we could cut that shorter, fewer people would get so ill and fewer would die once on treatment. The real problem unfortunately is that I think this study's subjects represent only the "tip of the iceberg," and that the majority of new smear positive pulmonary tuberculosis patients never show up at all. The study was not conducted on a larger scale because of time and resource constraints.

3.16 Budget support

This study was financed by Norwegian Association of Heart and Lung Patients (LHL), Norway.

3.17 Technical support

Technical support was obtained from International Union Against Tuberculosis and Lung Disease (The Union) France, LHL, Norway, and Chulalongkorn University (Faculty of Medicine, College of Population Studies, and College of Public Health), Thailand.