CHAPTER III

RESEARCH METHODOLOGY

3.1 Research Design

Retrospective cohort study was designed as I recruited persons who were HIV-infected TB patients. I carried out the cohort study retrospectively because it is more convenient, safe time, and safe resources, although it has its own limitations that will be addressed later.

3.2 Research setting

The setting of the study is An Giang province in southwestern Vietnam, with population of 2,120,000 (An Giang report on HIV, 2005). The HIV prevalence among TB patients in An Giang was 3.6% in 2004, compared with the National HIV prevalence among TB patients was 4.6% in 2004 sentinel surveillance report (Vietnam Ministry of Health, 2004). Successful treatment rate and death rate among overall TB patients were 92% and 2.5% in the national report, respectively (WHO, 2006).

3.3 Research Population

Subjects included 1) all HIV-infected patients with TB diagnosed through chest radiography (CXR) screening and/or clinical assessment other than CXR screening; and 2) all TB patients were tested for HIV, and those with a confirmed HIV diagnosis (Ministry of Health guidelines, 2004) were included. All patients were followed up for at least eight months until completing TB treatment or until they died. I followed up all patients treated in 2004 until they treatment outcomes were identified.

3.4 Data source

With approval from leaders of An Giang provincial Department of Health, I and other co-investigators were able to review records from all TB and HIV program patients aged 15 years and above seen in the Preventive Medicine Center of An Giang province from 2001 to 2004. TB diagnosis is made by acid fast bacilli (AFB) smear microscopy and/or chest radiography. District health centers provide HIV screening tests through HIV program. These centers also provide AFB smear and chest x-ray screening to diagnose TB through TB program. HIV confirmatory testing for clients diagnosed through district TB health centers in An Giang is performed at the Preventive Medicine Center. Result of chest x-ray screening is also confirmed at the Preventive Medicine Center. HIV testing in the laboratory is by enzyme-linked immunosorbent assay (Genscreen, Sanofi, Paris, France or Serodia, Fujirebio, Tokyo, Japan) followed by two different HIV ELISA tests if the first is positive (the exact tests used varied over the time of this project).

From 2001 – 2004, HIV-infected patients enrolled in An Giang's home-based care program were also regularly referred for chest radiography to screen for pulmonary TB, regardless of symptoms.

3.5 Data Collection

Working with advisors from the Field Epidemiology Training Program (FETP), Ministry of Public Health of Thailand, a structured questionnaire was developed (see Appendix B) in order to facilitate data collection from the multiple registries and forms available. Data were abstracted from:

- *TB patient records at the provincial level*: TB suspected symptom, AFB smear findings, date of started TB treatment, case disease status (pulmonary smear-positive, pulmonary smear-negative, extra-pulmonary, new, re-treatment, or transfer-in), treatment regiment, adverse events during treatment, date stopped TB treatment, final treatment outcome (cured, treatment completed, treatment failure, died, defaulted, or transferred out), and previous history of TB treatment
- *Chest radiography reports*: getting chest x-ray, date of chest x-ray, and result of chest x-ray
- *HIV/AIDS patient clinical charts at district level*: personal and demographic data, HIV risk factors, date of HIV diagnosis, HIV related symptoms, getting co-trimoxazole, and getting ARV.

TB treatment categories were combined into a dichotomous variable of successful treament outcome (cure and completion) versus unsuccessful treatment outcome (death, failure and default), transferred out was excluded.

I divided age into five categories 15-24, 25-34, 35- 44, 45-54, 55-64 and greater than 65. We divided districts into "urban" (Long Xuyen city and Chau Doc district) or "rural" (the remaining nine districts).

TB clinical records indicated whether or not the patient suffered an adverse event during TB treatment. Clinical staff did not use a standardized definition for recording adverse events, and there was no supplemental documentation for what adverse event occurred. Staff reported that this category was most commonly used to indicate rash or intolerance to anti-TB medications.

HIV/AIDS clinical records collected data about occupation, education, religion, ethnicity, marital status, and HIV risk group using pre-specified options. I used these data elements and response options when collecting data. Patients were considered "unemployed" if they had no job, were a housewife, or were only intermittently employed. Education was classified as secondary or below (including illiterate persons) vs. high school or above (including college or university).

HIV risk assessment categories that were pre-defined on public health forms included: men who have sex with men (MSM), sex with a commercial sex worker (CSW), sex with a stable partner, sex with multiple partners, heterosexual sex with

spouse, injection drug user (IDU), HIV-infected mother (i.e., mother-to-child transmission), or others.

HIV/AIDS clinical records included whether a patient had symptoms consistent with HIV at the time of HIV diagnosis. These symptoms included: weight loss > 10%, fever > 1 month, diarrhea > 1 month, TB, Candida esophagitis, neurological disorder, recurrent pneumonia, invasive cervical cancer, cryptococcal meningitis, Kaposi's sarcoma, generalized herpes infection, or others. I divided data about the presence of HIV symptoms into "yes" if any HIV symptom was noted (including other write-in symptoms) or "no."

HIV/AIDS clinical records also indicated whether a patient was prescribed co-trimoxazole (CTX). Records did not indicate, however, the dosage, frequency, or duration of CTX and whether the patient actually ingested the drug. An Giang HIV/AIDS program policy is to provide CTX to all HIV-infected persons free of charge. ART was not available in An Giang province during the years covered by this evaluation.

3.6 Training for all evaluation personnel and pre-test of questionnaire

A one-day training session was held at the province level for all research assistants to explain the purpose of this evaluation, familiarize them with the data abstraction form, and answer questions or concerns related to the evaluation. The questionnaire was reviewed by FETP advisors for clarification. I was present for the

initial weeks of data abstraction and data entry in order to address additional queries that arise during the course of the evaluation.

3.7 Data Analysis

Data was entered into Microsoft Access version 2000 as data can be managed effectively and also be easily transferred to other statistic programs. The data then transfer to SAS version 9.1 and SPSS version 13.1 for analyses. Univariate analyses were used to describe mean median, range of age and proportions of age, gender, occupation, education, HIV risk factors, HIV related symptoms history of TB treatment, TB disease status, symptoms at TB diagnosis, and final TB treatment outcomes. Bivariate analyses were used to show differences in proportions of successful and unsuccessful treatment outcomes according to TB diagnostic category by using T-test for continuous data and the Chi-square test for categorical variables. I compared HIV-infected TB patients with successful TB treatment outcome to those with unsuccessful outcome. In bivariate analyses, I analyzed risk factors for unsuccessful outcome by age, sex, occupation, education, marital status, HIV risk group, residence in a rural district, adverse event during TB treatment, CPT, prior history of TB, TB types, and registration status.

Most of the reference categories were selected because a majority of patients fell under the categories. Some of the reference categories were selected based on the selection of other studies.

In multivariable logistic regression analyses, I selected variables for inclusion based on plausibility, *a priori* evidence, completeness of data, and/or a p-value <=.20 in bivariate analysis.

There were 3 models developed. The first module included adverse event during TB treatment, resident in rural area, pulmonary smear-negative TB vs. pulmonary smear-positive, CPT and male gender, age and year of treatment of the patients. CPT missing was re-coded as having received Co-trimoxazole and put into model 2. In addition, I re-coded CPT missing as not received Co-trimoxazole and put into model 3.

3.8 Ethical review

CDC and the Vietnam NTP determined that this evaluation represented a public health program evaluation, not human subjects research, and, therefore, did not require a review by an institutional review board.