CHAPTER 3

METHODOLOGY

Research designs, scope and methods

The major goal of this study was to describe the adherence of Thai ALWHs and taking antiretroviral therapy at the age of 10-18 years. This study consisted of three phases. In phase I, a qualitative study was used to understand the attitudes and beliefs about disease and medicine among ALWHs. EM, HBM and TPB were used for developing the study's theoretical framework. Focus group discussion (FGD) and in-depth interview were used to collect data.

In phase II, results from Phase I and literature review were used to develop a questionnaire acquiring information about factors affecting adherence with ART for ALWHs. For attitudes and beliefs, the researcher collected data by distributing the questionnaire to HIV-infected adolescents. Adherence was determined by pill count and interview. Then, findings were analyzed for assessing major predictors for adherence in adolescents.

In phase III, predicting factors gained from phase II were put together with the individual patient's contents in order to develop a tailored program for enhancing ART adherence of adolescents infected with HIV. Finally, the researcher evaluated the program for its effectiveness in improving adherence, knowledge and CD4 cell count.

The research was conducted primarily at Surin Hospital in phase I. Potential participants for study Phase II will also include those HIV-infected adolescents at Northern and North-Eastern regions, Thailand. In phase III, the research was conducted at Surin Hospital again. This study's methodology could be described in three phases as follow.

3.1 Phase I: A qualitative study to describe the explanation, attitudes and beliefs about disease and medicine.

The aim of this phase was to describe the explanation, attitudes and beliefs about disease and medicine in the perspective of ALWHs and receiving antiretroviral therapy. From the literature review, there is a limited research focus on this group of patients living in Thailand. To seek information for answering this goal, a qualitative research method was used.

3.1.1 Objective: To describe the attitudes and beliefs about health and medicine in the perspective of ALWHs and receiving antiretroviral therapy.

3.1.2 Research design: A focus group discussion method was employed to collect attitudes and beliefs of participants. An in-depth interview was used in cases of sensitive information.

3.1.3 Population and Sample

The study population was Thai adolescents living in Surin Province. They were prenatally infected with HIV-1 and had been taking antiretroviral therapy for at least 1 year at the age of 10-18 years. The study's sample was patients receiving HIV treatment at Surin Hospital at the time of study and eligible for the study.

Study inclusion criteria: The patients were asked to participate in the study if they had the following characteristics.

1. Were willing to participate in the study. They voluntarily gave an informed consent. Additionally, since they were children who were a vulnerable group, it was required to gain an informed consent from their guardian such as, parent, grandmother, grandfather, or other relatives.

2. Prenatally HIV-1 infected

3. Had already disclosed about their infection status

4. Aged between 10-18 years

5. Had been taking ART for at least 1 year

6. Followed up at immunology clinic, Surin Hospital during August – September 2012

3.1.4 Data Collecting Tools

Data collection tool was a list of questions to be asked in the focus group discussion and in-depth interview. The questions included the items in the constructs of EM, HBM and TPB. EM was used to explain how the patients perceive their illness and the ART medicines. Additionally the interview gathered information about HBM constructs including how the patients perceive their conditions regarding severity and susceptibility. They were asked about barriers and benefits of ART adherence. These HBM constructs served as an attitude towards the behavior in TPB. Based on TPB, other constructs collected were subjective norms, perceived behavioral control and intention to comply with ART adherence. Results from this phase were used to construct questions to be included in the questionnaire as the tool of data collection in phase II.

The content analysis was assessed by three expert opinions. There were two university faculties who had experience in health behavior research and another one was a pediatrician and had experience in treatment of children /adolescents with HIV-infection at immunology clinic. Comments gained from the experts were used to re-check with models and theory concepts and literature review. Then, the questions were modified regarding the comments. The researcher used the questions to pretest with five adolescents at immunology clinic, Surin Hospital to affirm their validity. The final questions were developed according to feedback data from the pretest.

The topic guide for assessing knowledge, attitudes and beliefs about HIV/ AIDS disease and medicine in this study included these following aspects:

Knowledge of disease and medicine

Cause of HIV/AIDS

How is HIV-infection transmitted from one person to another?

What do you think about HIV progression?

Severity of HIV/AIDS

What do you think about the difference between HIV-infection and AIDS?

What make you fear about this disease?

Treatment of HIV/AIDS

Why can antiretroviral drugs help you?

What kind of HIV/AIDS treatment do you think you should receive?

What are the most important results you hope to receive from HIV/AIDS treatment?

Attitudes and beliefs about disease and medicine

Perceived severity of the disease

What are the worst things that can happen to HIV/AIDS patients?

Can you die from HIV/AIDS?

Can HIV/AIDs be cured by anti-retroviral treatment?

Perceived risk of HIV drug resistance

Can drug resistance make your disease more complicated?

What will happen, if you take antiretroviral drugs too late or forget to take the drugs?

Perceived barriers to antiretroviral treatment

Do you have any transportation problems for coming to the hospital?

Have you ever had antiretroviral drugs side effects which are intolerable?

What are the barriers in taking antiretroviral drugs regularly?

Perceived benefits of treatment with antiretroviral drugs

Do antiretroviral drugs have a positive effect on your health?

Environment that affects adherence with antiretroviral drug therapy

What are your family's opinions about your disease?

What are your friends' and teachers' opinions about your disease?

What are your cousins' opinions about your disease?

What do you want from the doctor or healthcare team to improve your adherence?

What make you feel good in taking medication?

What are factors towards having negative feelings about taking medication?

What is the level of your intention to take your medication at the right time?

Perceived behavioral control

Can you personally control for yourself in taking medicine regularly?

Intention

What is the level of your intention to take medication at the right time ?

3.1.5 Data Collection Method

Purposive sampling method was conducted for this study. Data was collected at the immunology clinic, Surin hospital. The clinic runs every Tuesday. Person living with HIV/AIDS who work as volunteers at the clinic described details of the study for

guardians and adolescents who met the study's inclusion criteria while they were waiting to see the doctor. Potential participants and their guardians were informed about the research project. Those who agreed to participate in the project will be asked to sign the assent and consent form. Only those whose inform consents gained from themselves and their guardians were invited to participate in the study.

The focus group discussion (FGD) was conducted with 6-8 participants in the room. The modulator of group discussion was a person living with HIV/AIDS who works as volunteer at the clinic. They were chosen because they had close contact with this group. The researcher served as a note taker. If participants had depression or other signs for psychological harm between focus group interventions, the modulator and their team work would take care them until they calmed down. In cases of sensitive cases with those having psychological difficulties and difficulties in disclosing HIV status, data was collected by in-depth interview. The data was collected until it reached saturation or no additional information was gained from the interview.

There were three rounds of FGDs, one in-depth interview in a separate room was conducted at the end of discussion. The discussion took 25 – 40 minutes for each session. Information gathered from the discussion and in-depth interview was analyzed. At the end of each round, the findings and working hypotheses gained from the first group were shared with the modulator in order to develop questions to be asked in the next group session. The second and third FGDs were taken at 2 weeks and 4 weeks after the first FGD. After the third FGD, there were no new relevant data obtained, data saturation was reached.

3.1.6 Data Analysis

Data collected from field notes and voice recorder was analyzed though content analysis. All FDGs and Interviews were audio taped and transcribed verbatim. Content analysis includes these following steps was used for analyzing the qualitative data. (Elizabeth et al., 2006):

1. Reading for overall understanding

2. Coding qualitative data. Codes were tags or labels, which were assigned to whole documents to help catalogue key concepts while preserving the context in which these concepts occur.

3. Developing the code structure by using a well-crafted, clear and comprehensive code structure.

4. Using grounded theory approach to developing code structure. Data was reviewed line by line in detail and as a concept becomes apparent, a code was assigned. Upon further review of data, the researcher continued to assign codes that reflect the concepts that emerge, highlighting and coding lines, paragraphs, or segments that illustrate the chosen concept. As more data was reviewed, the specifications of codes were developed and refined to fit the data.

5. More deductive approaches to developing code structure

6. The codes and code structure were finalized at the point of theoretical saturation. This was the point at which no new concepts emerge from the reviewing of successive data from a theoretically sensitive sample of participants.

3.1.7 Ethical Consideration

In sample recruitment, potential participants and their guardians were informed about the research project. They were able to ask any questions that they had and the researcher would answer in order to clarify any concerns of the patients and their guardians. Those agreed to participate in the project were asked to sign the assent and consent form. Only those whose inform consents gained from themselves and their guardians were invited to participate to the study.

In data collection, their name, hospital ID or any personal identification were not shown on the records. Study ID was used to identify the participants. Every piece of information collected in this study was protected from access by other people by using password protected electronic files and backup files. Only the researcher gained access to any written documents which kept in a closed and locked cabinet at home. These data would be deleted five years after the study.

In data presentation, no personal identification was presented. The findings described the opinions and information of the group. In case for example, the researcher will present as the study ID will be assigned for each individual by the researcher. This study received ethics approval from the Ethical Committee of Surin Hospital.

3.2 Phase II : A quantitative study to identify factors affecting adherence

In phase II, the results from Phase I and literature review were used to develop a questionnaire which served as the study's data collection tool. Additionally, some clinical data was collected.

3.2.1 Objectives: This phase was aimed to identify factors affecting adherence with antiretroviral therapy for adolescents living with HIV and receiving antiretroviral therapy.

3.2.2 Research design: A cross-sectional study using a survey and a clinical data collection form.

3.2.3 Population and Sample: Population for this study was adolescents infected with HIV/AIDS and taking antiretroviral therapy at the age of 10-18 years that follow up at public hospitals in the Northern and North-Eastern of Thailand. Samples were adolescents aged 10-18 years who were prenatally HIV-1 infected and had been taking ART for at least 1 year at immunology clinics in public hospital in Chiang Mai, Lampang, Tak, Kamphaengphet, Surin, Buriram and Roiet.

The sample size was calculated by the number of factors needed for regression analysis which was the major analytical method used in this study. It required minimum of 10 participants per predictor variable (Green's, 1991) plus 50 (Harris, 1985). Since we expected to have 32 factors to be studied, we need an estimation of sample size as followed;

$$\text{At least sample size} = (10 * \text{number of predictors}) + 50$$

$$= (10 \times 32) + 50$$

= 320 + 50

= 370 cases

The minimum number of sample size for this phase was 370 cases. To account to less than 100% response rate which was a limitation of survey research, an additional 5% of the samples were added. An additional 19 individuals was needed, resulting in a total sample size of 389 patients.

The patients were asked to participate in the study if they had these following characteristics.

1. Were willing to participate in the study. They voluntarily gave informed consent. Additionally, since they are children who are a vulnerable group, it is required to gain an informed consent from their guardian such as, parent, grandmother, grandfather, or other relatives.
2. Prenatally HIV-1 infected
3. Had already disclosed about their infection status
4. Aged between 10-18 years
5. Had been taking ART for at least 1 year
6. Followed up at immunology clinics at public hospitals in Chiang Mai, Lampang, Tak Province, Kamphaengphet, Surin, Buriram and Roiet during the study period (December 2013 – July 2014).

Multistage sampling method was used. First sampling method used was proportional sampling. The number of ALWHs in each site and total number of samples were used to calculate the proportion of the samples of the Northern and North-Eastern regions. The number of adolescents infected with HIV/AIDS and taking antiretroviral therapy at the age of 10-18 years (population) in Thailand as followed (NHSO Thailand, 2012);

1. Northern Provinces 967 cases
2. North-Eastern Provinces 1,667 cases

Total 2,634 cases

This made the proportion of cases by region as 37: 63 (of Northern provinces: North-eastern provinces) and the modified number of cases was 144: 245 from Northern and North-eastern parts of Thailand, respectively.

Then, convenience sampling method (together with snow ball technique) was used. The researcher, first, contacted a hospitals' HIV care team to participate the study. If the HIV-clinic coordinators were willing to participate the study, the researcher went to visit the site and collected the data from ALWHs following up at that hospital. The researcher, then, asked for any further contacted with their co-ordinating hospitals that might be interested to participate the study from the coordinator. The researcher contacted the next HIV-clinic coordinator and collected the data until reached the sample size. By using this technique, the numbers of cases from each site were:

1. Northern Provinces (total 144 cases)

1.1 Chiang Mai Province Hospitals	96 cases
1.2 Lampang Province Hospitals	6 cases
1.3 Tak Province Hospitals	8 cases
1.4 Kamphaengphet Province Hospitals	34 cases
total	144 cases

2. North-Eastern Provinces (total 245 cases)

2.1 Surin Province	160 cases
2.2 Buriram Province	45 cases
2.3 Roiet Province	40 cases
total	245 cases

3.2.4 Data Collection Tools: Data collection tools were questionnaire and a clinical data collection form.

1. Questionnaire

Results from phase I study showed the difference knowledge of ALWHs and could be classified into two age groups. Then, the questionnaire was classified into

two forms, there were an early adolescents (age 10 – 15 years) form and a middle adolescents (age 16 – 18 years) form. It had the same structure. The only difference was in the words “CD4” and “Viral load” were use in middle adolescent form, where as “healthy” and “weak” were use in early adolescent form. It contained three parts;

1.1 Demographic data

This part consisted of closed-end check list questions to assess gender, age, availability of caregiver, number of parent alive, transportation convenience and education, friend disclosure status and community disclosure status. The opened-end questions were used to ask about participant’ s caregiver, family income per month, number of HIV positive family members (e.g. parent, sister or brother), number of friends and community disclosure.

1.2 Attitudes, beliefs and knowledge about disease and medicine

This part of the questionnaire included questions asking about attitudes, beliefs and knowledge as mentioned in Phase I. Words and sentences used by sample patients in Phase I were used to develop items asked in this Phase. They consisted of constructs listed in the explanation and knowledge about disease and medicine, perceived susceptibility, perceived severity, perceived barriers, perceived benefits, subjective norm, perceived behavioral control and intention to regularly take antiretroviral drugs. The 5-point Likert-type scale was used for questions regarding attitudes and beliefs.

A true-false type question with a total of 22 items was used for assessing their knowledge of disease and medicine. It consists of three domains of knowledge; transmission, progression and treatment and medicine.

1.3 Others

In addition, the questionnaire was collect additional information regarding stigma and discrimination. The items asked were a 5-point Likert-type scale

which is defined into five levels; strongly disagree, disagree, not sure, agree and strongly agree.

To develop a user-friendly questionnaire, each question in the questionnaire must be clear, short and easy to understand. To ascertain about quality of data collection tools, content analysis and a reliability test were used. Content validity was reviewed by three experts who work closely in the area of HIV, adolescent, and behavioral science. Then the questionnaire was adjusted according to their feedback. A reliability test was conducted by trying out the questionnaire with 30 ALWHs in immunology clinic at Buriram Hospital. The conbrach's alpha was used to assess the questionnaire reliability. The acceptable alpha conbrachs 'coefficient reliability test was at least 0.7. The following was a summary of all steps for questionnaire development in phase II.

1. Developed questionnaire, using data from the Phase I study and literature review.

2. Checked for content analysis from 3 experts (the same team as phase I study).

3. Adjusted survey form followed by the instructions from experts.

4. Pretested the questionnaire with 30 ALWHs at Surin Hospital and check for reliability and factor loading.

5. Revised the questionnaire based on the test values and pretest the questionnaire again until the test values were satisfactory.

Developing the questionnaire by these steps, the final questionnaire gained reliability of 0.79 for attitudes and beliefs and 0.81 for knowledge about disease and medicine among early adolescents, assessed by conbrachs' coefficient. Reliability for middle adolescents was at 0.78 for attitudes and beliefs and 0.70 for knowledge about disease and medicine.

2. Clinical Data Collection Form

Clinical data collection form was used for gathering clinical data from the participants. It was completed by a healthcare team or volunteer who were taking care of the participants. Data regarding antiretroviral drugs included; gender, age, age at started ART, CD4 at date of starting ART, duration of ART, ART regimen, ADR experience, number of pills taken per meal, number of times taken per day, depression risk level, and drug resistance status. Additionally, the form asked about participant's complete pill count record and adherences interview.

Content validity of clinical data collection form was reviewed by three experts who work in the area of HIV-infected adolescents and behavioral science. It was tried out with 5 healthcare teams or volunteers at Surin Hospital for its clarity and case of use. Finally, it was revised according to the experts' suggestion and the results from received data In summary, types of independent variables and resources are described in table 2.

Table 3.1 Types of independent variables and resources

Variables	**Type**	**Resource**
Demographic data		
1.Gender (male/ female)	Discrete	Questionnaire
2.Age (year)	Continuous	Questionnaire
3.Caregiver (yes/ no)	Discrete	Questionnaire
4.Family income (baht)	Continuous	Questionnaire
5.Transportation difficulties (yes/ no)	Continuous	Questionnaire
6.Studying status (yes/no)	Discrete	Questionnaire
Clinical data		
1.Age at ART was started (year)	Continuous	Medical records
2.ART Duration (month)	Continuous	Medical records
3.Regimen (first line/second line)	Discrete	Medical records
4.Number of pill/meal	Continuous	Medical records
5.Drug resistance (yes/no)	Discrete	Medical records
6.CD4 at date of starting ART	Continuous	Medical records

Table 3.1 (Continued)

Variables	Type	Resource
(cell/cubic millimeter)		
7.Opportunistic Infection Status (Never/ Ever/ Current)	Discrete	Medical records
Knowledge of disease and medicine		
1. Transmission* (score)	Continuous	Questionnaire
2. Progression* (score)	Continuous	Questionnaire
3. Treatment and medicine* (score)	Continuous	Questionnaire
4. Total knowledge* (summary score)	Continuous	Questionnaire
Psychosocial factors		
1.Percieved susceptibility** (score)	Continuous	Questionnaire
2.Perceived severity** (score)	Continuous	Questionnaire
3.Perceived benefits** (score)	Continuous	Questionnaire
4.Perceived barriers** (score)	Continuous	Questionnaire
5.Cues to action** (score)	Continuous	Questionnaire
6.Self-efficacy** (score)	Continuous	Questionnaire
7.Subjective norm*** (score)	Continuous	Questionnaire
8.Perceived behavioral control*** (score)	Continuous	Questionnaire
Other factors		
1.Stigma*** (score)	Continuous	Questionnaire
2.Discrimination*** (score)	Continuous	Questionnaire
3.Friend disclosure*** (yes/no)	Discrete	Questionnaire
4.Community disclosure*** (yes/no)	Discrete	Questionnaire
Intention		
Intention to ART adherence* (score)	Continuous	Questionnaire
ART adherence		
Adherence (yes/no)	Discrete	Medical records

* Questionnaire develop by researcher

** Questionnaire adopt from HBM (Rosenstock, Strecher & Becker, 1994)

*** Questionnaire adopt from TPB (Ajzen, 1991)

3.2.5 Data Collection Method

The questionnaire was answered by a total of 389 participants from 30 sites of study. There were 9 sites from Northern region: Chiang Mai Province (Maharaj Nakorn Chiang Mai, Sanpatong, Hangdong, Sarapee and Doisaket), Kamphaengphet Province (Kamphaengphet and Phrankratai), Tak Province (Somdejprajaotaksinmaharaj), Lampang Province (Thoen) and 21 sites from North-Eastern region: Surin province (Surin, Prasat, Kabchoeng, Sangkha, Sikhoraphum, Thatoom, Samrongthap, Lamduan, Chomphra, Rattanaburi and Sanom), Buriram province (Prakhonchai, Nangrong, Lam Plai Mat, Huairat, Plabplachai, Krasang and Satuek), Roiet province (Roiet, Suwannaphum, Selaphum).

For distributing questionnaires and clinical data collection forms to the data collecting sites, the researcher contacted the HIV-clinic coordinator at each site in order to explain the study objective and data collection process. Additionally, they provided the manual guide describing how to collect data. If they were unsure about any steps of data collection, they could directly contact the researcher by mobile phone at all times.

The coordinator asked the patients who meet the inclusion criteria to participate to the study. The researcher explained the objectives of the study and asks for their participation. The patient who agrees to join the study would voluntarily give out an informed consent. Also, an informed consent from their guardian such as, parent, grandmother, grandfather, or other relative was gained. Participants who had problems in reading and/or understanding the research questions were able to ask the healthcare team or volunteer at the site to read and explain the question to them. Finally, the researcher collected the questionnaires from all sites.

3.2.6 Data Analysis

Descriptive statistics analysis using percentage and frequency were employed for analyzing categorical data such as gender, availability of care giver and transportation difficulty.

Mean and standard deviation (S.D.) were used for analyzing numerical data such as age, family income per month, duration of ART and CD4 cell counts at start date of ART.

Adherence for each participant was calculated by using average percentage of pill count adherence in the last two visits and confirmed with an interview record.

$$\% \text{ Adherence} = \frac{(\text{initial stock} + \text{refilled amount}) - \text{final stock} \times 100}{\text{Number of pills/day} \times \text{Number of follow-up days}}$$

If the interview data does not correlate with the pill count data, adherence was calculated from interview data, therefore from percentage proportion of number corrected doses taken and total doses, as below;

$$\text{Adherence (\%)} = \frac{\text{Number of correct doses taken}}{\text{Number of total doses}}$$

Number of correct doses taken = number of doses taken right (not more than 30 minutes too late and not forgotten) from interviewed data

Number of total doses = number of times taken per day **x** duration from last visit to evaluate day (days)

Finally, adherence was defined into two levels for regression analysis;

Adherence = ≥ 95%

Non-adherence = less than 95%

To assess factors associated with adherence, multiple logistic regression analysis was used. In multiple logistic regression (Aldrich & John, 2005), several independent or predictor variables and a dependent or criterion variable.

In this study, independent variables were classified into 6 groups; demographic data (6 variables), clinical data (7 variables), knowledge of disease and medicine (4 variables), psychosocial (8 variables), others (4 variables) and intention (1 variables).

Dependent variable was adherence (adherence/ non-adherence). For knowledge about disease and medicine, the third quartile was used as a cut point to classify the knowledge into two group (high and low to moderate knowledge).

First, univariate analysis for each independent variable was analyzed in order to select only significant varibles ($p < 0.05$) into the multiple logistic regression models. Multiple logistic regression analysis was used to predict the independent effect of a variable on dependent variables of interest; which are intention to ART adherence and ART adherence. At the end of Phase II, a list of factors that significantly influence adherence were developed and considered in the development of a program in Phase III.

3.2.7 Ethical Consideration

To protect the participants from any possibility of harm, the researcher complied with the participants' rights of protection. The questionnaire and the clinical data collection form were linked together by using the study code. Study coordinator in each site assigned the study code for each participant. The data from the questionnaire and the clinical data collection tool were matched together by the researcher. Thus, the name of participants, hospital ID, and other personal information must be concealed. The collected documents were kept in a locked cabinet at an office where only the researcher and project coordinators could access. Electronic files and backup files with password protected and were stored in the researcher's personal computer. No personal data was presented in the final research reported.

Phase II study received ethics approval from the Ethical Review Committee of the Faculty of Pharmacy, Chiang Mai University, the Ethical Review Committee of the Faculty of Medicine, Chiang Mai University and the Ethical Committee of Surin Hospital.

3.3 Phase III: A quasi-experimental design to develop an intervention program aimed to improve ART adherence

In Phase III, the researcher developed an intervention into the real life situation. Findings from Phase I and II were used to develop an intervention program aimed to

improve ART adherence and treatment effectiveness among the ALWHs. Then, an only significantly predictive variable was used to develop a pilot intervention to improve patient's adherence in study Phase III.

In addition, data from several studies highlighted that caregivers (Santer et al., 2014; Sivapalasingam et al., 2014; Usitalo et al., 2014; Ugwu & Eneh, 2013; Udompanich et al., 2008; Azmeraw & Wasie, 2012) and family support (Santer et al., 2014; Mellins et al., 2004;) were associated with ART adherence. Intervention to support caregivers were important for caring process in children and adolescents (Busza et al., 2014; Mutwa et al., 2013; Azmeraw & Wasie, 2012; Merzel et al., 2008; Nicholson et al., 2006).

Moreover, results from phase I presented the interesting that family played major role on their normative belief, anti-retroviral drugs' side-effects and physical properties and their activities during the time taking antiretroviral drugs were common individualize barriers to antiretroviral drugs treatment. Phase II result was contributed to the association between caregiver and adherence. This consensus with the finding from previous studies that individualize interventions focusing on caregivers and adolescents should be prioritized for prevention and treatment efforts to address non adherence during the transition into adolescents (Naar-King et al., 2013; Reisner et al., 2013).

Therefore, the researcher decided to develop an intervention which targeted to the context of individual caregivers and ALWHs. To do so, an individual home visit was used for intervention implementation, instead of a group activity at hospital clinic.

3.3.1 Objectives

1. To develop an intervention program for improving adherence of the adolescents living with HIV and receiving antiretroviral therapy.

2. To assess the effectiveness of the intervention in improving adherence of the adolescents living with HIV and receiving antiretroviral therapy.

3.3.2 Research design

Quasi-experimental design was used. The independent variable was an intervention program. The dependent variable was ART adherence, knowledge about disease and medicine and CD4 cell count.

3.3.3 Methods

Findings from Phase II provided significant factors influencing adolescents' adherence to ART. Finding from Phase I supported the reasons and explanations of the relationship between the factors. These findings were used for designing an appropriate intervention program for improving medical adherence of Thai ALWHs. The most practical intervention program was examined with the regular patient care at Surin Hospital. Additionally, the researcher assessed the effectiveness of the program after intervention.

Phase III study was designed to pilot test the developed intervention with ALWHs at Surin Hospital. It was an individual tailored intervention where the researcher, as a pharmacist responsible for HIV clinic at Surin Hospital, took a visit to the ALWHs' house. The goal of first visit was to investigate the target individualize caregiver's problems and ALWHs' problems related to ART adherence together with the participant' family. Then telephone contacts were used in consecutive one month later for second and third visits. Quasi-experimental design by pre- and post-test was used for evaluating the outcomes of the intervention. The second and third visits were actions at one month period after the first and second visit, respectively. The study was conducted during August to November 2014.

Step of intervention in first visit (home visit)

1. Introduced the researcher and explained the objective of phase III study to participants' family member

2. In depth interviewed with participant

3. In depth interviewed with caregiver (if available)

4. If the data not completed, searched for other key informants

5. Assessed for problems related to ART adherence together with the participant and their family

6. Gave individual recommendation or intervention

7. Telephone contacted in consecutive one month after home visit for second and third follow up.

3.3.4 Hypothesis:

There were a difference of ART adherence, knowledge about disease and medicine and CD4 cell count between before and after the intervention program.

3.3.5 Population and Sample: Population were adolescents infected with HIV and taking antiretroviral therapy at the age of 10-18 years that follow up at immunology clinic, Surin Hospital. Study samples were adolescents who have these following characteristics.

1. Were willing to participate in the study. They voluntarily gave informed consent. Additionally, since they were children who were in a vulnerable group, it was required to gain informed consent from their guardian such as, parent, grandmother, grandfather, or other relatives.

2. Prenatally HIV-1 infected

3. Had already disclosed about their infection status

4. Aged between 10-18 years

5. Had been taking ART for at least 1 year

6. Followed up at immunology clinic, Surin Hospital during August to September 2014.

7. Had been identified as non-adherence for the last two visits.

Data from the literature review were used to calculate sample size by G Power 3.1.3 program which is available for free download on the internet. Then following demand for test, means, two dependent group (matched pairs), respectively. After input variables data were completed, program was calculated the sample size.

1. An intervention aimed for improving adherence by a brief intervention from pharmacist (Malow et al., 1998). Input variables for effect size calculation were mean adherence before intervention (M_1) = 48, standard deviation before intervention (SD_1) = 16, mean adherence after intervention (M_2) = 75, standard deviation after intervention (SD_2) = 21, output data showed effect size = 0.59, then G Power 3.1.3 Input variables were two tails, effect size = 0.59, α error probability = 0.20, power (1-β error probability) = 0.80. Output data showed the main result for total sample size = 9 and additional 2 samples (20% of total sample size) for loss to follow up, then 11 samples were used.

2. An intervention aimed for improving adherence by life steps (a single-session intervention utilizing cognitive-behavioral, motivational interviewing, and problem-solving techniques) and medication monitoring to patients who were considered at risk for adherence problems (Steven et al., 2001). Input variables for effect size calculation were mean adherence before intervention (M_1) = 74, standard deviation before intervention (SD_1) = 28, mean adherence after intervention (M_2) = 95, standard deviation after intervention (SD_2) = 7, output data showed effect size = 0.46, then G Power 3.1.3 Input variables were two tails, effect size = 0.46, α error probability = 0.20, power (1-β error probability) = 0.80. Output data showed the main result for total sample size = 14 and additional 3 samples (20% of total sample size) for loss to follow up, then 17 samples were used.

Therefore, 17 samples were used for phase III study since it required a larger sample size.

3.3.6 Data Collection Tools

Data collection tools were a form designed to collected respondents; adherence, knowledge about disease and medicine and CD4 cell count. Primary outcomes or ART

adherence was measured at week 0 (baseline) and week 8 (post-intervention). Secondary outcomes are knowledge about disease and medicine, CD4 cell count which also be measured at the baseline and 8-weeks after the intervention. ART adherence was measured by pill count method and interviews for missed doses 7 days prior (similar to the method mentioned in phase II study). Knowledge about disease and medicine was measured by questionnaires. The following data collection tools were used;

1. Demographic data and clinical data collection form

The form was used to collect participant's gender, age, ART regimen, drug resistant status, duration of ART and CD4 cell count at the baseline and after the intervention. This information were gathered from patient's records by the researcher who is also a pharmacist responsible for HIV-infected adolescents at the site.

2. Adherence data collection form

The form was used by the researcher to get information about amount of medicines ordered and retained. Additionally, it was used for recoding the interview for missed doses 7 days prior (the same as in study Phase II)

3. Questionnaires for assessing knowledge about disease and medicine

Items in the questionnaire were used to assess participant's knowledge about disease and medicine. It was the same questionnaire used in study Phase II. Therefore, content validity and reliability of the questionnaire were warranted.

3.3.7 Data Collection Method

The potential participants were recruited at an immunology clinic, Surin hospital which runs every Tuesday. Potential participants and their guardians were informed about the research project. Those who agree to participate in the project were asked to sign the assent and consent form. Only those with consent gained from the individual and their guardian were invited to enroll on this study.

At the baseline (week 0), the researcher was collected ART adherence and CD4 cell count at the prior visit. Demographic data and clinical data collection forms, adherence data collection form were completed. Participants were asked to answer questions assessing their adherence and the questionnaire assessing knowledge about disease and medicine.

At the first visit, the researcher and a person living with HIV/AIDS working as a volunteer at the immunology clinic, Surin hospital who was familiar with participants' family went to visit the participants at their house. Participants and their family members were interviewed by a researcher. During the interview, the researcher assessed their living context, needs and problems related to ART adherence. Information gained from the interview was used for designing a specific intervention for the participants. Intervention could be any recommendation or accommodation that would help the participant overcoming their barriers to ART adherence. Specifically, the intervention focused on clarifying any misunderstood points that the caregivers or ALWHs or their family members had; encouraging caregivers or family members to help with medicines preparation and reminder; addressing any concerns the caregivers or ALWHs or their family had; and making sure that the patients were able to attend their responsibilities. In the case of not having caregiver, the researcher was decided individual intervention on ALWHs or their family members based on their needs.

The second and third visit was designed for following up the outcomes of the intervention. It was done by either home visit or telephone interview. Outcomes of the intervention ART adherence, knowledge score and CD4 cell counts. At the second visit (week 8 after the intervention), the participants will be asked to answer the questionnaire for assessing knowledge by themselves again. The researcher will collect ART adherence and CD4 cell count again.

3.3.8 Data Analysis

Primary outcome for this phase is to improve ART adherence, secondary outcomes are knowledge of disease and medicine and CD4 cell count.

Descriptive statistical analysis in percentage and frequency were used to analyze samples' demographic data. Inferential statistical analysis was used to test for the program's effectiveness. Dependent t-test was used to compare adherence and knowledge score. Wilcoxon's rank test was used to compare CD4 cell count before and after the intervention.

3.3.9 Ethical consideration

In sample recruitment, potential participants and their guardians were informed about the research project. They were able to ask any questions that they had and the researcher would answer in order to clarify any concerns of the patients and their guardians. Those who agreed to participate in the project were asked to sign the assent and consent form. Only those whose inform consents gained from themselves and their guardians were invited to participate to the study.

In data collection, their name, hospital ID or any personal identification were not presented on the records. Study ID were used to identify the participants. Every piece of information collected in this study was protected from access by other people by using password protected electronic files and backup files. Only the researcher would gain access to any written documents which were kept in a closed and locked cabinet at the office and would be deleted after the study had ended for 5 years.

In data presentation, no personal identification was presented. The findings would describe only the opinions and information of the group. In case for example, the researcher would presented as the study ID Phase III study received ethics approval from the Ethical Review Committee of the Faculty of Pharmacy, Chiang Mai University and the Ethical Committee of Surin Hospital.

Conceptual framework

Conceptual frameworks for 3 phases of this study were shown in figure 3.1–3.3

Adolescents living with HIV/AIDS

1. Explanation about disease and medicine
2. Attitudes toward to comply with ART adherence

   (Perceived severity, susceptibility, barriers, benefit)
3. Subjective norm

   3.1 Normative beliefs

   3.2 Motivate to comply with ART adherence
4. Perceived behavioral control
5. Intention to comply with ART adherence

Figure 3.1 Conceptual framework of Phase I study

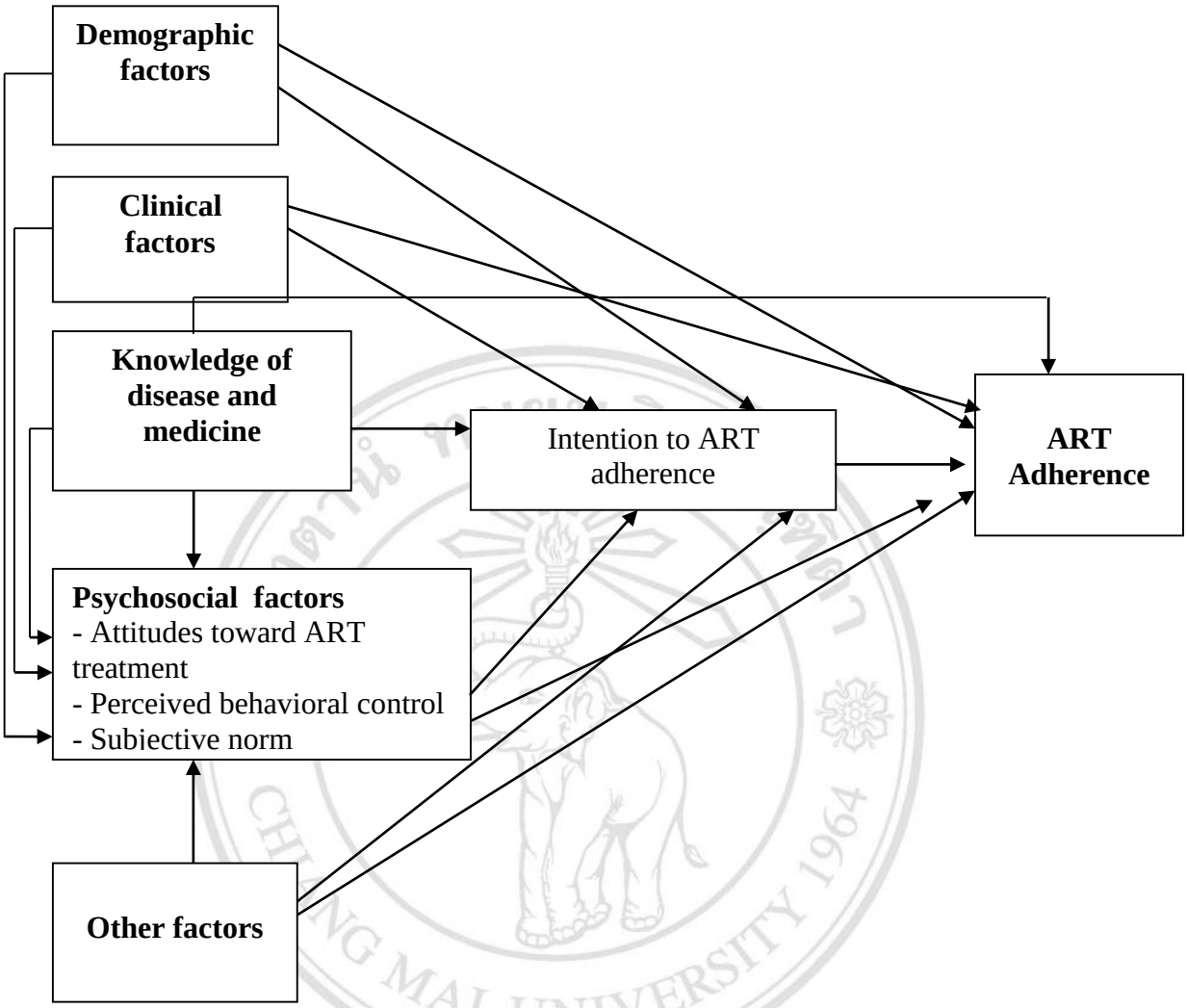

Figure 3.2 Conceptual framework of Phase II study

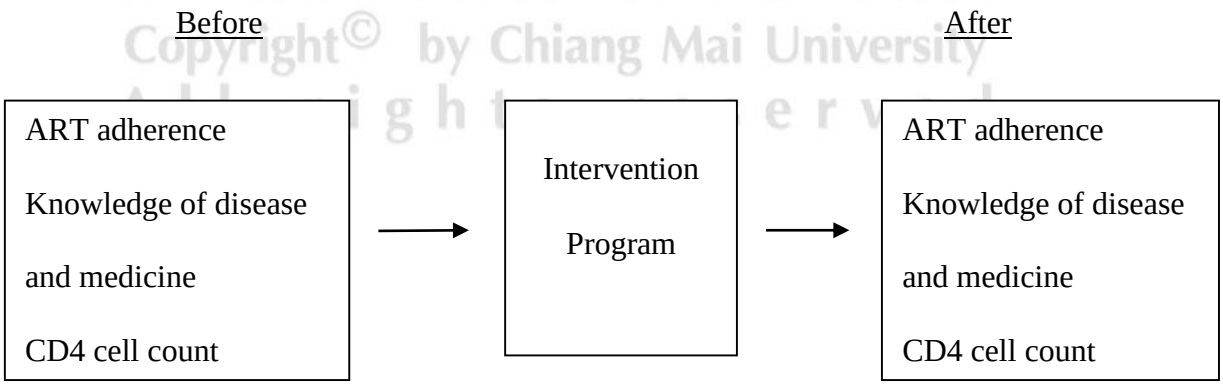

Figure 3.3 Conceptual framework of Phase III study