BARRIERS TO ADHERENCE OF HIV/AIDS PATIENTS TO ANTIRETROVIRAL THERAPY AT SIHANOUK HOSPITAL CENTER OF HOPE, PHNOM PENH, CAMBODIA

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TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ACRONYMS AND ABBREVIATIONS

ABC	Abacavir
AIDS	Acquired Immune Deficiency Syndrome
APU	Ritsumeikan Asia Pacific University
ART	Anti-retroviral Therapy
ARV	Anti- retroviral
AZT	Zidovudine
DDI	Didanosine
D4T	Stavudine
EFV	Efavirenz
3TC	Lamivudine
GDP	Gross Domestic Product
IDU	Injecting Drug Users
HAART	Highly Active Anti-Retroviral Therapy
HIV	Human Immuno-deficiency Virus
JICA	Japan International Cooperation Agency
JICE	Japan International Cooperation Center
KALETRA	Lopinavir/ritonavir
MoH	Ministry of Health
MSM	Men who have Sex with Men
NAA	National AIDS Authority
NCHADS	National Center for HIV/AIDS, Dermatology and STDs

NVP	Nevirapine
NGO	Non-Governmental Organization
NNRTI	Non-Nucleoside Reverse Transcriptase Inhibitor
NRTI	Nucleoside Analogue Reverse Transcriptase Inhibitor
OI	Opportunistic Infection
PCP	Pneumocystis Carinii Pneumonia
PI	Protease Inhibitor
PLWHA	People Living With HIV and AIDS
PMTCT	Prevention of Mother to Child Transmission
RCAPS	Ritsumeikan Center for Asia Pacific Studies
SHCH	Sihanouk Hospital Center of HOPE
STD	Sexually Transmitted Diseases
TB	Tuberculosis
TDF	Tenofovir
UNAIDS	Joint United Nations Program on HIV/AIDS
UNICEF	United Nations Children's Fund
USAIDS	United States Agency for International Development
US$	US Dollar
VAS	Visual Analogue Scale
VCCT	Voluntary Confidential Counseling and Testing
WHO	World Health Organization
WB	World Bank

ABSTRACT

Introduction

According to UNAIDS/WHO (2009), HIV/AIDS is a global problem that needs to be addressed. Universal access to antiretroviral therapy (ART) has been expanded significantly in both low and middle-income countries. To achieve the effectiveness of antiretroviral therapy, adherence to ART must be optimal ($\geq 95\%$) and maintained for life. However, adherence to antiretroviral therapy is difficult to reach this optimal goal and faces many problems, especially in resource-poor settings. In 2007, Cambodia had approximately 75,000 adults and children living with HIV, including 0.8% of all adults aged from 15-49 years. The Ministry of Health of Cambodia through the National Center for HIV/AIDS, Dermatology, and STDs (NCHADS) has expanded ART program coverage substantially. The number of people living with HIV/AIDS patients on ART has increased by 40 percent, from 26,664 in 2007 to 37,315 in 2009. Also, the number of HIV/AIDS patients on ART at Sihanouk Hospital Center of HOPE has increased to 2467 by March 30, 2010. Since the number of HIV/AIDS patients on ART has increased dramatically, ART adherence of patients must be good in order to achieve effectiveness of the treatment. The objectives of this study were to discover barriers to adherence to antiretroviral therapy of HIV/AIDS patients at Sihanouk Hospital Center of HOPE.

Methods

The study was conducted at Sihanouk Hospital Center of HOPE between August 16, 2010 and September 30, 2010. The study design was cross-sectional in the form of a

case-control study of poor ART adherent and good ART adherent patients, which employed both qualitative and quantitative approaches. Purposive and simple random sampling techniques were used in the study for recruiting poor ART adherent patients and good ART adherent patients respectively. Of 117 subjects selected for the study sample, 60 were poor ART adherent patients, while 57 were good ART adherent patients. Primary data were collected using face-to-face interviews through the author-administered and structured questionnaire. Secondary data were collected using cohort data in order to identify poor ART adherent patients and good ART adherent patients among all HIV/AIDS patients who were receiving highly active antiretroviral therapy (HARRT) through the Visual Analogue Scale (VAS) at the Infectious Disease Department of Sihanouk Hospital Center of HOPE. Moreover, the secondary data were collected through a variety of other sources in a bid to find out relevant documents, information, and previous research findings. Data were coded and analyzed using SPSS version 18, and a Chi-square test was used to identify an association between dependent and independent categorical variables.

Results

Results of data analysis show that the majority (93%) of the total 117 research respondents are good ART adherent patients, while seven percent are poor ART adherent patients. The reasons for missing ART doses cited by research respondents were forgetfulness (22.2%), being busy, conflicts with family and neighbors, lack of time reminders such as alarm clocks and cell phones, altogether 35.9%, being too ill (6%), fear of stigma/disclosure (6%), drunk with alcohol (5.1%), feeling better (2.6%), developed

toxicity/side effects (2.6%), too many pills/pill burden (2.6%), and stock was finished (1.7%). Univariate data analysis shows that ART side effects were statistically significantly associated with poor ART adherence (X^2=7.150, df =1, P-value=0.007). Types of ART regimens, co-opportunistic infection drug treatments, knowledge of ART, educational levels, patient's location of residence, and poverty status were not significantly associated with poor ART adherence. Other factors such as gender, age groups, CD4 groups, WHO stages, marital status, occupations, and food status were not significant predictors for poor ART adherence.

Conclusions

It was concluded that most of the research respondents (93%) were good ART adherent patients, while seven percent were poor ART adherent patients. The factors for poor ART adherence cited by research respondents were forgetfulness, being busy, lack of time reminders, being too ill, fear of stigma/disclosure, drunk with alcohol, feeling better, side effects, and the pill burden. ART side effects were significantly associated with poor ART adherence, while ART drug regimens, co-infection drug treatments, HIV/AIDS disease factors, and socio-demographic and economic factors were not significantly associated with poor ART adherence.

Based on the findings above, in order to enhance ART adherence, the Cambodian government and other stakeholders could take stronger measures to reduce and manage ART side effects by providing education and training to clinicians, counselors, nurses, and pharmacists. Furthermore, the government, through the Ministry of Health, could intensify health education campaigns against stigma and discrimination and promote family and

community support for HIV/AIDS patients, and provide patients with time reminders such as alarm clocks. The findings of this study could be an important resource for ART program managers and policy makers attempting to achieve the success of antiretroviral therapy.

CHAPTER I: INTRODUCTION

1.1. Rationale of the study

<u>1.1.1. Background</u>

This section provides detailed situation of HIV/AIDS in general and situation of HIV/AIDS in Cambodia.

1.1.1.1. Situation of HIV/AIDS in general

Human Immunodeficiency Virus (HIV) is a virus that can enter the human body by different modes of transmissions such as sexual intercourses, intravenous drug injections, blood transfusion, needle and syringe injuries, breast-feeding, and mother-to-child transmissions. When an HIV is inside the human body, it multiplies rapidly, attacks and kills immunity-system-protecting-lymphocytic T cells such as macrophages and especially CD4; later on, the numbers of CD4 will decrease substantially. People infected with HIV can develop Acquired Immune Deficiency Syndrome (AIDS), a condition in which their immune system begins to fail, leading to life threatening opportunistic infections such as respiratory diseases, skin diseases, sexually transmitted diseases, gastro-intestinal diseases (specifically diarrhea), lymphatic system diseases, tuberculosis, and nervous system diseases such as meningitis.

HIV/AIDS is one of the most serious diseases that cannot be cured and it causes many problems to people living all over the world, especially in the developing countries, of Sub-Saharan Africa, South and South-East Asia. HIV/AIDS

produces serious and negative socio-economic impacts on individuals, households, communities, and nations. When one HIV-infected person becomes an AIDS patient, he or she suffers from a lack of immunity and poor quality of life. As a result, he or she cannot study, work, or earn enough money to support himself or herself, let alone his or her family. Moreover, he or she cannot participate in other socio-economic activities in the community as well as the country and finally he or she encounters poverty. In addition, if one country has many HIV/AIDS patients, it faces a shortage of human resources because of the high morbidity and mortality of the patients and the country needs to spend a large amount of money on HIV/AIDS patients' prevention, treatment, care, support, and other related management. Therefore, the country may be unable to build and develop the nation. Hence, poverty ensues. HIV infections have spread from one country to another and from one continent to another to create a world pandemic.

Since the beginning of the epidemic, almost 60 million people have been infected with HIV and 25 million people have died of HIV/AIDS-related causes. In 2008, about 33.4 million people were living with HIV/AIDS (PLWHA) and 2.7 million new infections occurred. The number of these new infections was approximately 30 percent lower than the number for 1996, which appears to be a peak year for such infections. There was also a significant decrease in the number of AIDS related deaths, from 3.5 million in 1996 to 2.1 million in 2008 [Joint United Nations Program on HIV/AIDS (UNAIDS)/ World Health Organization (WHO), 2009)]. The

estimated worldwide adult (15-49) HIV prevalence was around 0.9%. Of the total 33.4 million PLWHA, adults and children less than 15 years account for 31.3 million and 2.1 million respectively. 15.7 million out of the 31.3 million adult HIV patients were women. In the same year, 2008, the number of HIV infected children globally was 2.7 million and young people accounted for approximately 40 percent of all new adult (older than 15) HIV infections. In Sub-Saharan Africa, PLWHA accounted for 67 percent of the total HIV infected patients and 91 percent of all new infections among children in the world (UNAIDS/WHO, 2009). Worldwide, the HIV epidemic is mainly caused by heterosexual intercourse, which accounts for greater than 75 percent (Matte, Lajoie, Lacaille, Zijenah, Ward, & Roger, 2004). The second mode of HIV transmission is homosexual intercourse (Volk et al., 2006) and the third mode/route of transmission is through unsafe drug injections amongs drug users which varies from country to country (Hope et al., 2005).

The level of HIV prevention in the world is still limited. In 2008, the percentage of pregnant women infected with HIV receiving antiretroviral therapy for prevention of mother to child transmission of HIV (PMTCT) increased from 33% in 2007 to 45% in 2008. However, less than 40% of young people had basic information on HIV and the same percentage of people living with HIV/AIDS know their HIV status (UNAIDS/WHO, 2009). Though there are international campaigns for HIV prevention, care, treatment, and support, the number of new infections still exceeds the number of HIV/AIDS patients on Antiretroviral Therapy (ART). For every two

people starting treatment, a further five become infected with the virus, because while on antiretroviral medications, the quality of life of patients receiving treatment improves and thus they transmit the disease to others (UNAIDS/WHO, 2009).

Globally, the number of people living with HIV/AIDS in need of ART is approximately 9.5 million. However, only close to four million patients have received ART, which accounts for 42% coverage of adult patients and 38% of children in low and middle-income countries, which still remains low compared with the number of patients who require ART (UNAIDS/WHO, 2009).

Having access to ART has a significant impact on HIV related deaths. For example, a multicenter study of 12 high-income countries indicates that the excess rate of mortality among PLWHA, compared with the HIV uninfected population, dropped by 85 percent owing to the introduction of highly active antiretroviral therapy (HAART) (Bhaskaran et al., 2008). However, the decline in AIDS related deaths due to successful ART contributed to an increase in HIV prevalence in high-income countries (Center of Disease Control and Prevention, 2008). Moreover, HAART has increased the survival of PLWHA in low and middle-income countries. For instance, a study in Sao Paulo, Brazil shows that average survival increased from four months in 1991-1995 to 50 months in 1998-2001 (Kilsztajn, Lopes, Do Carmo, & Rocha, 2007). In the same year, 2008, the number of people living with HIV/AIDS in Sub-Saharan Africa was 22.4 million, equaled 5.2% adult HIV prevalence rate; new HIV infections, AIDS related deaths, and AIDS orphans were 1.9, 1.4, and 14

million respectively. In addition, among 6.7 million people in need of ART, only 2.9 million have received ART, which accounted for 44% of ART coverage of HIV/AIDS patients in the region (UNAIDS/WHO, 2009).

Since the epidemic started, the disease has continued to ravage families, communities, and countries throughout the world. Consequently, many people infected with HIV/AIDS were unable to work, make their living and engage in other activities; eventually they have died. In response to this shocking situation, the international communities, local organizations, civil societies, and the governments have taken serious actions in fighting together against the outbreak of the HIV/AIDS disease. These measures include Voluntary Confidential Counseling and Testing (VCCT) of HIV, HIV preventions, home-based care, opportunistic infection treatments, antiretroviral therapy, and other related managements.

With the strong effort and struggle of local and international communities in response to the HIV/AIDS epidemic and the enormous number of deaths of AIDS patients, the number of people living with HIV/AIDS worldwide had declined to 33.4 million by 2008. Of these, 22.4 million were in Sub-Saharan Africa and 4.7 million in Asia, of which 3.8 million PLWHA were in South and South-East Asia (UNAIDS/WHO, 2009).

According to UNAIDS/WHO (2009), the number of people living with HIV/AIDS in Asia in 2008 was 4.7 million. There were 350,000 new adult infections and 21,000 new children infections and there were 330,000 AIDS related deaths. The

estimated regional adult (15-49) HIV prevalence was about 0.3%. The HIV annual incidence has dropped by more than half; the regional epidemic peaked in the mid-1990s and has remained nearly stable since 2000. Even though the annual number of deaths related to AIDS in South and South-East Asia in 2008 was about 12 percent lower than the number of AIDS deaths in 2004, the AIDS-related mortality rate in Asia continues to rise, with the number of deaths in 2008 more than three times higher than that in 2000.

The epidemic patterns of HIV infections in the region have a wide variation. In fact, Asian population is very diversified and large, which represents about 60 percent of the world population. The number of people living with HIV/AIDS in Asia is high, second only to Sub-Saharan Africa, in comparison with worldwide PLWHA. India contains about half of Asia's HIV prevalence. Moreover, all countries in Asia, except for Thailand, had HIV prevalence less than 1 %. Due to the large population in the region, although Asia's HIV prevalence is low, the number of HIV patients still contributes to a large proportion of the HIV burden on the globe (UNAIDS/WHO, 2009). As of 2007 in China, the number of PLWHA was 700,000, new infections 50,000 and AIDS related deaths 20,000 (Wang et al, 2009). Furthermore, epidemic of HIV in Asia has been mainly focused on the most-at-risk population of HIV infections such as injecting drug users, sex workers as well as their clients, and Men who have sex with Men (MSM). In general, injecting drugs and sexual contact, especially heterosexual contact, are still the primary modes of HIV transmission in

China and Asia (Wang et al., 2009). In the Asian region, injecting drug users are among people who have the highest HIV prevalence, which accounted for about 16%. However, the HIV prevalence of this high-risk population varies substantially from one country to another country (Mathers et al., 2008).

Even though the estimated annual number of new HIV infections in South and South-East Asia declined from 450,000 in 2001 to 340,000 in 2007, most South-East Asian countries, especially Indonesia, had an increase in HIV prevalence. The increasing number of new infections made Indonesia the site of the fastest growing epidemic in Asia despite the fact that the national HIV prevalence was low, 0.16 percent; and the total number of people living with HIV/AIDS was 193,000 as of 2006 (World Health Organization, 2007). Moreover, the primary modes of HIV transmission in Indonesia were injecting drug use, unprotected paid sex, and unprotected sex between men (Ministry of Health of Indonesia, 2006). In Thailand, in 2004, the number of people living with HIV/AIDS was 572,500, new HIV infections 19,500, and projected new AIDS cases 49,500. Sexual contact, especially heterosexual, has remained the primary mode of HIV transmission in Thailand (Rueankham, 2008). The number of people living with HIV/AIDS in Vietnam in 2007 was estimated to be 293,000, which equaled 0.53 % prevalence in the general population. It was estimated that 28.4% of PLWHA were on ART in 2007. HIV infections in Vietnam are primarily among the most-at-risk populations such as injecting drug users, female sex workers, and men who have sex with men (MSM)

(National consensus workshop on United Nations General Assembly Special Session on HIV/AIDS, 2008). In Lao's People Democratic Republic in 2009, people living with HIV/AIDS accounted for 8,000, which equaled 0.2 % prevalence rate among 15-49 years old population. Since 2006, the ART coverage of HIV/AIDS patients in this country has increased to 92%. The major modes of HIV transmission in this country (87%) were due to heterosexual contact, followed by unknown sources 6.5%, and mother-to-child transmission 4.6% (National Committee on the Control of AIDS, 2010).

Despite low HIV prevalence, the economic impact and consequences of HIV/AIDS will put an additional six million households in Asia into poverty by 2015 if national and regional responses are not made and strengthened significantly and effectively (Commission on AIDS in Asia, 2008). 38% of all HIV/AIDS patients in need of ARVs in Asia were receiving ART, just below the global coverage (42%) in low and middle-income countries by the end of 2008, which represents a seven-time increase in ART access over five years (UNAIDS/WHO, 2009). Though Asia has made much progress in HIV prevention and ARV treatment, many countries cannot afford to provide enough priority to HIV prevention. Prevention of high-risk behaviors is still a concern (National AIDS commission, 2006-2007).

1.1.1.2. Situation of HIV/AIDS in Cambodia

Cambodia has been the victims of a civil war, which lasted over 30 years. The wars, especially the one that occurred during the Pol Pot (Khmer Rouge) regime,

destroyed almost all the infrastructure, human as well as natural resources, properties, other valuable belongings, and particularly the health care system. The health care system of Cambodia, the worst in Asia, was completely demolished such as hospital amenities, equipments, medical supply, and health care personnel. After the Pol Pot regime ended in 1979, few health care providers had survived; there were 45 medical doctors (however, 20 of them left the country), 26 pharmacists, 28 dentists, and 728 medical students (Laura & McGrew, 1990). As a result, Cambodia has become the poorest country in the South East Asia region. Cambodia's Gross Domestic Product (GDP) per capita was US$ 610 (1US$=4000 Riel, local currency) and 30.1 percent of the total population, 14,805,358 millions, were living below the poverty line, earning less than 1US$ per day (World Bank, 2009).

In 2008, life expectancy of Cambodian people at birth was 59 years for men and 65 years for women; neonatal mortality rate per 1,000 live births was 48; infant and under 5 mortality rate per 1,000 live births was 71 for males and 58 for females and 89 for male and 75 for female respectively. Adult mortality rate per 1,000 population was 371 for male and 301 for female; and maternal mortality ratio per 100,000 live births was 540 (WHO, 2008).

The educational level of Cambodian people is still limited. In 2007, the adult literacy rate was about 75 percent, women and men accounted for 66 and 85 percent respectively. Generally, people living in the capital city, Phnom Penh, have higher education than those living in other urban and rural areas. Moreover, men have a

higher educational level than that of women in both urban and rural areas (National Institute of Statistics Ministry of Planning, 2007).

Figure 1.1: 15 year-and-over adult literacy rate by geographical areas and sex, 2007
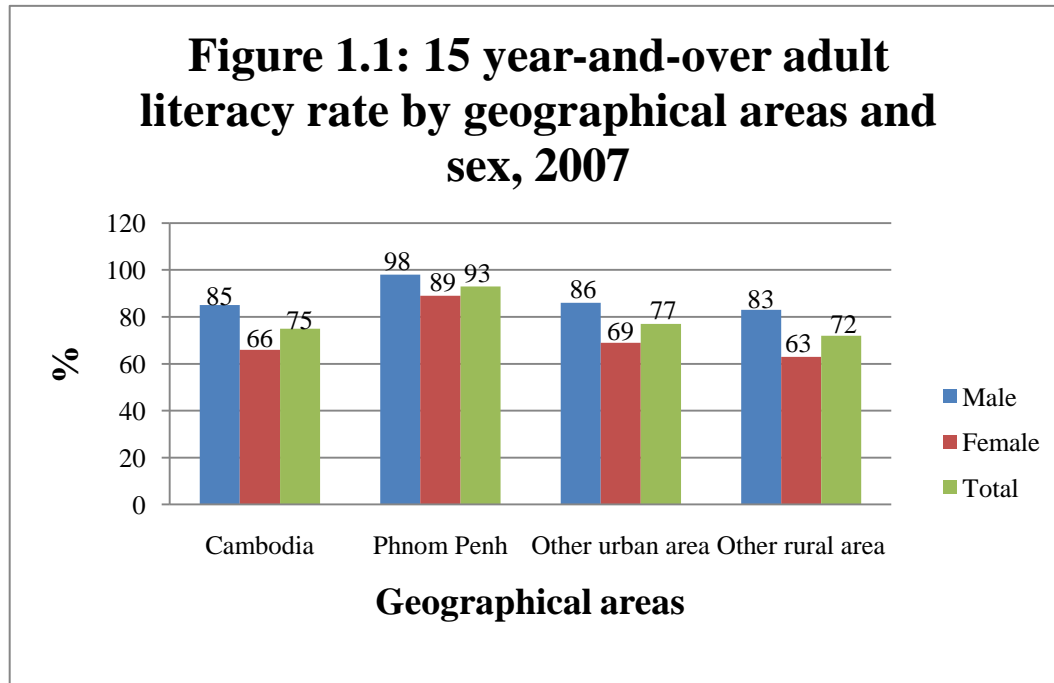
Source: Cambodia socio- economic survey, 2007. National Institute of Statistics, Ministry of Planning

Among people aged 25 years and over, 37 percent of women and 15 percent of men had no education or had not finished first grade. The number of women and men who did not complete primary school was similar. In particular, the higher the level of a school, the lower the number of women enrolled (National Institute of Statistics Ministry of Planning, 2007).

Figure 1.2: Persons aged 25 years and over by educational attainment and sex, 2007
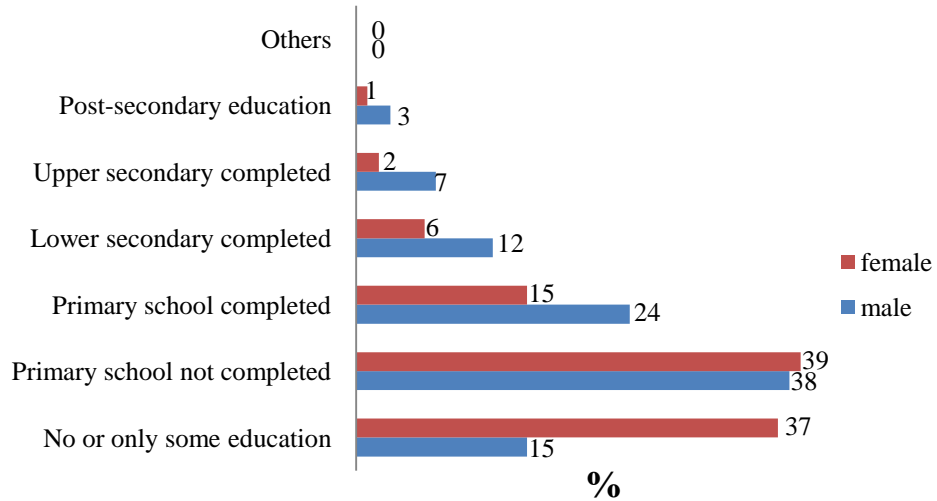
Source: Cambodian Socio-Economic Survey, 2007. National Institute of

Statistics, Ministry of Planning

Such low educational attainments are most likely to make people more vulnerable to diseases since education and health conditions have links to each other. There is a negative association between lower educational level and HIV infections; this means that when people have lower educational background, they are more likely to have HIV infections (Piot, Bartos, Ghys, Walker, & Schwartländer, 2001).

According to the National Center for HIV/AIDS, Dermatology, and STDs (NCHADS) (2000), the first HIV infection was reported to the National Blood

Transfusion Center in Phnom Penh in 1991. Later, the first case of AIDS was detected and reported to the Ministry of Health of Cambodia in 1993.

Figure 1.3: HIV prevalence in South-East Asian countries
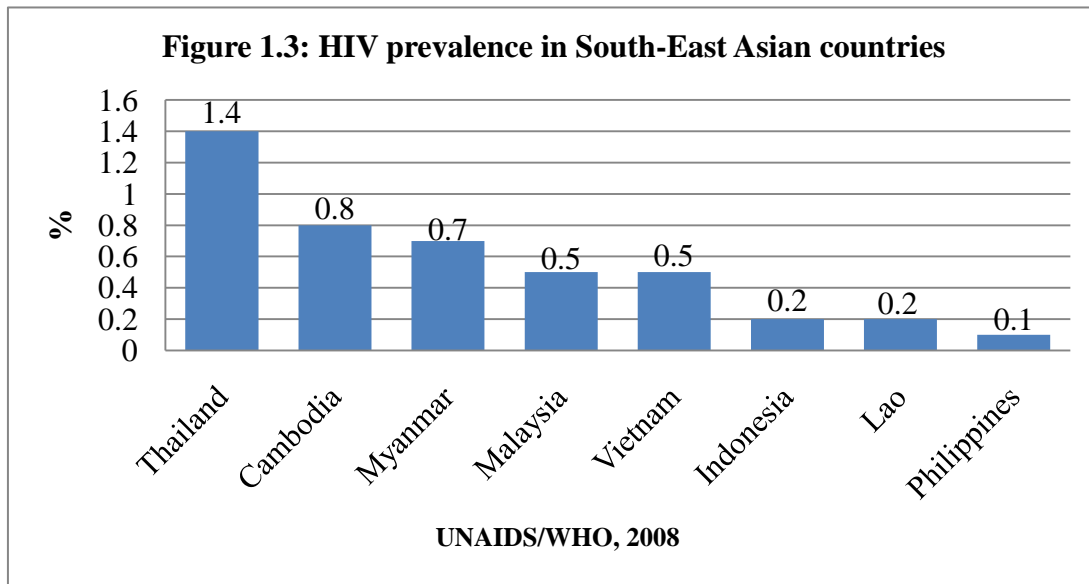
UNAIDS/WHO (2007) and National Center for HIV/AIDS, Dermatology, and STDs (NCHADS)'s estimates (2008) showed that Cambodia had one of the most serious HIV epidemics with 0.8 percent HIV prevalence, second only to Thailand, with 1.4 percent HIV prevalence among Southeast Asian countries. There were approximately 75,000 adults and children with HIV in 2007, about 0.8% of adults aged from 15-49 years old had HIV infection, and the number of AIDS related deaths was 6,900 (NCHADS, 2008). Even though the prevalence of HIV in Cambodia had dropped from the peak 3.0% in 1997 to 1.9% in 2003 and 0.8% in 2007 (NCHADS, 2008), these figures cannot completely mean that new infections are decreasing as the drop in prevalence may result from the deaths of long-term AIDS cases and it is still

the second highest in the region. It is estimated that the HIV prevalence will continue to decline from the current level (0.8%) before 2011 if the interventions are sustained. A resurgence of the HIV epidemic, however, cannot be ruled out because of the risk of second wave of new infections among most-at-risk populations such as female direct and indirect sex workers, their clients and other sexual partners, men who have sex with men (MSM) and injecting drug users (IDUs) (National AIDS Authoriy, 2008).

National response to HIV epidemic has increased remarkably, which is the achievement of cooperation and coordination between the government and civil society, including local non-governmental organizations, international non-governmental organizations, UNAIDS, WHO, United Nations Children's Fund (UNICEF), and United States Agency for International Development (USAID). Moreover, NCHADS plays a leading role in fulfilling the national response in order to reverse the HIV epidemic. HIV prevention interventions among general populations in the country have increased significantly, especially those in target groups. For example, the number of sites for prevention of mother-to-child transmission of HIV (PMTCT) have expanded from 27 sites in 16 operational districts in 2005 to 98 sites in 58 operational districts in 2007 and to 200 sites in 67 operational districts in 2009 (National AIDS Authority, 2010). By 2009, 32.3 percent of the total 2475 HIV-infected pregnant women received ART in order to prevent transmission from mother to child, which increased from 1.2 percent in 2003 to 11.2

percent in 2007 (National AIDS Authority, 2010). Furthermore, health facilities that provide voluntary confidential counseling and testing (VCCT) have been increasing rapidly from 197 in 2007 to 233 in 2009 (National AIDS Authority, 2010). The number of people tested for HIV has risen dramatically from 212,789 in 2006 to 363,799 in 2009 (NCHADS, 2010). However, there has been no new available data on voluntary confidential counseling and testing (VCCT) among the general population, female sex workers and MSM or prevention programs for most at risk populations (National Institute of Statistics Ministry of Planning, 2008).

In order to achieve the universal access target, the Ministry of Health of Cambodia through NCHADS and civil society have worked together to expand the coverage of care, ARV treatment, and support services in 20 out of the 24 provinces of Cambodia. As a result, health facilities with ART services have increased substantially from 30 sites in 2005 to 52 sites in 2009 (National AIDS Authority, 2010). The number of people living with HIV/AIDS (PLWHA) in need of ART was 30,200 in 2009 and increased to 31,600 by 2010 (National AIDS Authority, 2008). Remarkably, the number of AIDS related deaths declined sharply from 9950 in 2006 to 1210 in 2009 owing to the impact of ART. This indicates that ART program had averted 8,740 deaths in the three-year period (NCHADS, 2007). ART program has scaled up significantly because the number of HIV/AIDS patients in need of ART, as well as, those on ART is increasing and the advantages of ART are well demonstrated. To achieve ART success, HIV/AIDS patients must have optimal/good

adherence (adherence equal to or greater than 95%) to ART. Good adherence is the key to the effectiveness of ART (Malangu, 2008), while sub-optimal/poor adherence (adherence less than 95%) is the main predictor of HIV drug resistance, ART failure, and patient's survival (Cauldbeck et al., 2009).

About 5% of PLWHA were on second-line ART and the resources required for total ART were US$ 4,142,800 (National AIDS Authority, 2008). Of this amount, US$ 1,409,360 was for second-line adult ART in 2009 and the resources required for 2010 increased up to US$ 4,336,800; from which US$ 1,409,360 was for second-line adult ART (National AIDS Authority, 2008). In addition, the costs of second-line ART are US$ 892/month which is about 10 times more expensive than those of first-line ART (US$ 92/month) (Discussion on first-line regimens and second-line regimens, 2008).

In Cambodia, overall adherence level is estimated to be 87% (National AIDS Authority, 2007). Another study on simplified assessment of antiretroviral adherence and prediction of virological efficacy in HIV-infected patients in Calmette hospital, Phnom Penh, Cambodia 2003 (Olivier et al., 2010) showed that the adherence level assessed by the Visual Analog Scale (VAS) method was 71%.

The HIV/AIDS Department of Sihanouk Hospital Center of HOPE (SHCH) is a private non-governmental organization, established in 1997 after an HIV/AIDS epidemic occurred in Phnom Penh, the Capital city of Cambodia. It provides health care services free of charge. Since 1997, the Department has been recognized as an

HIV/AIDS Center for treatment and training in terms of supporting the HIV/AIDS National program that consists of 52 health facilities with ART services for the entire country. Furthermore, Sihanouk Hospital Center of HOPE has been known for its better quality of management and care of HIV/AIDS but that level is not high enough to meet the needs of people living with HIV/AIDS. By March 2010, there were 2,467 PLWHA on ART; of these 2,373 (95%) were on first-line ART, while 94 (4%) were on second-line ART (Sopheak, 2010). Of the 2467 HIV/AIDS patients, 2426 VAS were done, within which, 75 (3%) patients had poor adherence (adherence< 95%) (Sopheak, 2010). VAS is one of the tools used to measure the patient's self-reported adherence to ART in the last month before it is done. For example, with an ART regimen which is taken twice daily, if a patient misses less than or equal to three doses per month means good adherence (adherence level $\geq$ 95%) while missing at least four doses per month means poor adherence (adherence level< 95%) (Soklida, 2101).

1.1.2. Literature review and problem statement

1.1.2.1. Overview

HIV/AIDS disease is not curable, however, it can be treated by Antiretroviral Therapy (ART) to prolong survival and improve the quality of life of patients. However, it requires adherence to a quite difficult regime of drugs for a lifetime. Adherence to ART is defined as sticking to the treatment plan by taking the correct dose of drugs at the correct time and in the correct way and follows dietary

restrictions and instructions such as food and fluid. It also means looking after drugs to make sure they are safe and effective to use (Castro, 2005). Another definition is that adherence to ART means taking the correct dose of medications, on schedule, and following dietary instructions (Maria, 2008). In general, these two definitions are used worldwide to define adherence to antiretroviral therapy. The former definition, on a broad perspective, sounds more precise than the latter one. One of the factors that contributes to successful treatment is that ART adherence level is optimal ($\geq$ 95%), which means that there is no more than three doses missed per month for a twice-time-daily regime (Keith, 2007). A rise in any levels of adherence to ART is associated with a decrease in disease progression. For example, a 10 % increase in the level of adherence to ART causes a 21% drop in disease progression (Nischal, Khopkar, & Saple, 2005). However, poor adherence is linked to the development of drug resistance, lower rate of increase in CD4 cell counts, undetectable viral load, therapeutic success, and increased hospital days, higher mortality rate, and leads to poor overall outcomes (Hogan & Salomon, 2005).

Non-adherence has been a global concern in many diseases, especially chronic ones. Adherence in chronic diseases is about 50 percent in developed countries; however, it is even lower in developing countries (World Health Organization, 2003). Similarly, adherence to antiretroviral therapy (ART) varies from 37 to 83 percent depending on drugs under study (Steel, Nwokike & Joshi, 2007). In addition, adherence levels vary from one study to another; more than 10 percent of patients

report missing at least one medication dose per day, while more than 33 percent report missing doses in the past two to four weeks (Chesney, 2000). Moreover, it is estimated that patients have taken their prescribed drugs about 50 percent incorrectly (Paterson et al., 2002).

Good adherence to ART in resource-poor settings is certainly achievable, but in some countries, it is difficult to verify it based on the follow-up data of the patients' compliance with treatment, which may not be available. Hence, it is hard to ascertain discontinuation of treatment, losses to follow-up and mortality (Hardon, et al., 2007).

1.1.2.2. Conceptual framework

Based on reviews of previous research, a conceptual framework was created. The diagram below demonstrates that people living with HIV/AIDS need to take antiretroviral drugs in order to survive and improve their quality of life. It also shows the outcomes of ART from both good adherence and poor adherence. Finally, the diagram indicates a variety of factors/barriers that can lead to poor adherence to antiretroviral therapy. This study focuses on identifying barriers to antiretroviral therapy adherence of the HIV/AIDS patients at Sihanouk Hospital Center of HOPE, Phnom Penh, Cambodia. The conceptual framework is divided into four main parts as follows: Antiretroviral therapy (ART), impacts of ART regimens on adherence, impacts of adherence on ART, and predictors of ART adherence.

Figure 1.4: Conceptual framework

HIV/AIDS patients → ART → Good adherence

Treatment regimens

ART side effects, ART regimens, co-opportunistic infection drug treatments

Patient factor

Socio-Demographic and Economic factors such as gender, age, marital status, occupation, education, poverty, food, knowledge on antiretroviral therapy

Disease characteristics

Opportunistic infections and HIV symptoms, WHO stages, and CD4

Clinical settings

Patient's location of residence from health settings

Other factors

Quality of life improved

ART success

Poor adherence

Low expenditure

HIV drug resistance

Contribution to country development

ART failure

More morbidity and mortality

High expenditure

More poverty

Source: Author

19

1.1.2.2.1. Antiretroviral therapy

Human Immuno-deficiency Virus (HIV) is a virus that enters the human body through a variety of modes of transmission such as sexual contact, injecting drug use, mother-to-child transmission, contaminated syringe and needle injury, and blood transfusion (Kenya National AIDS Control Council, 2009). While in human blood, HIV affects white blood cells, especially CD4 cells that protect and make the immune system strong. While HIV is in CD4 cells, it produces new copies, multiplies its numbers rapidly, and kills a number of CD4 cells. The immune system of HIV/AIDS patients, in fact, becomes weaker as CD4 cells decrease. Antiretroviral therapy is a treatment of choice for HIV/AIDS. It cannot cure this disease; however, it can prolong life and stop patients from being ill for many years. In reality, antiretroviral therapy plays a key role in slowing and reducing HIV reproduction and replication in blood (National Center for HIV/AIDS and STD Control Nepal, 2009). In order to be effective, ART requires HIV/AIDS patients to take at least three antiretroviral drugs together every day for a lifetime. Highly active antiretroviral therapy (HAART) is a treatment, which combines three or more ARVs. The general ART guideline recommends patients to take at least three drugs, except for the purpose of prevention of mother-to-child transmission; otherwise ART works for a short time, then it will not work, and finally the development of HIV drug resistance can occur (National Center of HIV/AIDS and STD Control Nepal, 2009). Antiretroviral drugs are classified, depending on which part of HIV replication they act on, into the following groups (World Health Organization, 2010).

- Nucleoside reverse transcriptase inhibitors (NRTI)

- Non-nucleoside reverse transcriptase inhibitor (NNRTI)

- Protease inhibitors (PI)

The overall goals of antiretroviral therapy are to improve quality of life of patients by restoring immune system function, reducing morbidity and mortality related to HIV/AIDS, and suppressing maximal and durable viral load. Also, the goals are to reduce and prevent ongoing HIV transmission (National AIDS and STI control programme, Ministry of Health, 2005).

1.1.2.2.2. Impact of ARV regimens on ART adherence

Almost all HIV/AIDS patients on ART need to take a regimen of three or more ARVs to achieve treatment success (Grierson, Bartos, de Visser & McDonald, 2000). Generally, the patient's adherence to ART seems to decline over time while on a regimen with a high pill burden, frequent dosing, frequency and severity of side effects, and complexity of drug regimens (Nakiyemba, Aurugai, Kwasa, & Oyabba, 2005). Moreover, fear and the presence of side effects also influence poor adherence (Nakiyemba, 1998). For example, metabolic reasons and gastro-intestinal symptoms account for 66 and 50 percent, respectively, influencing non-adherence (Cauldbeck et al., 2009). Dietary restriction of food and liquid is one of the main factors associated with poor adherence. It is known that some ARVs need to be taken on an empty stomach and others need to be taken after meals to adjust their ART time schedule making it hard for them to overcome drug intolerance (Nakiyemba, 1998). Some

ARVs have particular physical aspects and characteristics such as bigger tablet size as well as form and bitter taste, which discourage patients from taking their ARVs (Nakiyemba, Aurugai, Kwasa, & Oyabba, 2005).

1.1.2.2.3. Impacts of adherence on ART

While patients are on ART, two forms of adherence can occur: good adherence and poor adherence.

1.1.2.2.3.1. Good adherence

Good adherence to antiretroviral therapy provides optimal benefits such as maximum and durable viral suppression, increase in CD4, prevention of HIV drug resistance, promotion of immune recovery, decrease in morbidity and mortality, slowed disease progression, and thus, ART success (Steel, Nwokike, & Joshi, 2007). For example, one cohort study found that a mean increase in CD4 count of 83 and six cells/μL was associated with levels of adherence greater than 95 and less than 95 percent, respectively (Mannheimer, Friedland, Matts, Child, & Chesney, 2002). Another study on ART adherence of 76 HIV-infected patients showed that no patients with a level of adherence greater than 90% progressed to AIDS, compared with 8% of those whose level of adherence was 51-90% and 41% of those with a level of adherence less than 50% (García de Olalla, Knobel, Carmona, Guelar, López-Colomés, & Caylà, 2002). When ART success is achieved, the quality of life of HIV/AIDS patients is significantly improved and the expenses of HIV/AIDS related disease and other involved managements are even lower. In fact, the success of

antiretroviral therapy can reduce the expenditure and most importantly, it can contribute to the country's development.

1.1.2.2.3.2. Poor adherence

Unlike good adherence, poor adherence to ART in low- and middle-income countries is the most serious problem preventing the success of treatment (Markos, Worku, & Davey, 2008). Poor adherence leads to HIV drug resistance, antiretroviral therapy failure, high morbidity and mortality rate, increase in hospital stays as well as other HIV/AIDS related disease management practices, high expenditures, and even higher rates of poverty (Markos, Worku, & Davey, 2008). For instance, the cost of first line-ART adults is US$ 92 per person per month, while the cost of second-line ART adults is US$ 892, which is nearly ten times more expensive (National AIDS Authority, 2008). Furthermore, in 2007 the number of HIV/AIDS patients on second-line ART, which is used after first-line ART fails, in Cambodia was about five percent, however, it may increase in the following years due to the fact that more HIV/AIDS patients are currently on ART, and the number will also increase in the future (National AIDS Authority, 2008). Similarly, patients on second-line ART at Sihanouk Hospital Center of HOPE in 2010 were approximately 4 percent (Sopheak, 2010).

1.1.2.2.4. Predictors of adherence

According to literature reviews, there are many factors influencing adherence to ART. However, they belong to five main categories: treatment regimens, patient

factors, disease characteristics, clinical settings, and social factors such as family and community support, stigma and discrimination (Machtinger & Bangsberg, 2006).

1.1.2.2.4.1. Predictors related to treatment regimens

As mentioned previously, the complexity of drug regimens, frequent dosing, liquid and food restrictions, high pill burdens, and side effects are the key elements that lead to non-adherence. A study on antiretroviral therapy in Brazil found that prevalence of adherence was 75 percent; the study shows that more complex regimen of ART and high pill burdens were the main causes of poor adherence (Nemes, Carvalho, & Souza, 2004). Another study in Botswana revealed that prevalence was 77 percent. The factors that influenced non-adherence were side effects, complicated regimens, and the taste, size, frequent dosing, and high pill burdens, which included co-opportunistic infections drug treatment (Castro, 2005). Also, non-adherence was found to be associated with side effects in several studies as follows: The AIDS clinical trial group of 370 participants revealed that side effects were the strongest predictor of poor adherence (Ickovics & Meade, 2002). Another study in Ethiopia found that reporting symptoms and side effects in the last month before visits were associated with non-adherence (Markos, Worku, & Davey, 2008); another study in Bangalore, India showed that metabolic reasons and gastro-intestinal symptoms accounted for 66 and 50 percent, respectively, and were the main predictors of poor adherence to antiretroviral therapy; however, ART regimens were not statistically significantly associated with adherence (Cauldbeck, et al., 2009). ART pill burdens

including OI drugs were not significantly associated with poor adherence (Markos, Worku, & Davey, 2008; Zungu, 2009; Cauldbeck et al., 2009).

1.1.2.2.4.2. Predictors related to patient factors

Socio-demographic and economic factors of HIV/AIDS patients such as gender, age, marital status, occupation, education, poverty, food, knowledge and attitude about antiretroviral therapy, housing, and psychological problems are associated with poor adherence (Nemes, Carvalho & Souza, 2004; Machtinger & Bangsberg, 2006; Huong, 2009; Wanjohi, 2009). One study showed that factors associated with poor adherence to antiretroviral therapy were young age, low income, low literacy, unstable housing, and homelessness (Machtinger & Bangsberg, 2006). Furthermore, women busy taking care of their children and those with psychological problems were associated with poor adherence (Kennedy, Goggin, & Nollen, 2004). Another study on gay men found that about three-quarters of the partcipants reported missed doses in the last six months and approximately one-third missed a dose in the last week (Shernoff, 2001). However, some previous finding showed that gender was not associated with ART adherence (Orrell, Bangsberg, Badri, & Wood, 2003; Erah, & Arute, 2008). Low education is a factor that leads to poor adherence because, for example, when patients are illiterate, they cannot understand and remember the explanation of counselors and physicians and sometimes they take ARVs mistakenly (Piot, Bartos, Ghys, Walker, & Schwartländer, 200). Also, another study in Togo showed that treatment knowledge and cognitive demands related to complex ART

regimens are important components of adherence to ART (Potchoo, Tchamdja, Balogou, Pitche, Guissou, & Kassang, 2010). However, previous research findings show that education and knowledge of ART were not statistically significantly associated with adherence (Markos, Worku, & Davey, 2008; Cauldbeck et al., 2009). Another contrasting finding is that family income (poverty status) was not significantly associated with adherence to antiretroviral therapy (Orrell, Bangsberga, Badri, & Wood, 2003; Cauldbeck et al., 2009). Moreover, some previous findings found that occupations are not significantly associated with ART adherence (Orrell, Bangsberga, Badri, & Wood, 2003; Markos, Worku & Davey, 2008). One previous research found that food is not significantly associated with ART adherence (Manary, Ndekha, & Van Oosterhout, 2010).

1.1.2.2.4.3. Predictors related to disease characteristics

Disease characteristics such as duration of HIV/AIDS, opportunistic infections and its symptoms as well as morbidity, World Health Organization (WHO) stages, CD4, and viral load are predictors of non-adherence (Machtinger & Bangsberg, 2006). For example, a study on symptom management for improving quality of life and drug adherence in HIV/AIDS patients found that an increase in CD4 count and low or undetectable viral load were influencing adherence to antiretroviral therapy (Wood, Hogg, Yip, Harrigan, O'Shaughnessy, & Montaner, 2003; Chiou, Ing-Tiau Kuo, Lee, Chen, Chuang, & Lin, 2006). However, one previous research finding shows that CD4 count is not associated with ART

adherence (Erah & Arute, 2008; Ford, Darder, Spelman, Maclean, Mills & Boulle, 2010). The higher the severity of disease the more pain patients suffer, however, the lower adherence level patients have. For instance, higher severity of disease including, WHO stage 3 and stage 4, was associated with poor adherence (Shah, et al., 2007). However, some previous research findings found that WHO stages are not statistically associated with ART adherence (Orrell, Bangsberga, Badri, & Wood, 2003; Bajunirwe, Arts, Tisch, King, Debanne, & Sethi, 2009).

1.1.2.2.4.4. Predictors related to clinical settings

Clinical settings and health care services are one of the predictors of poor adherence. These include greater distances from health clinics to patients' homes and working places; difficult transportation conditions, such as bumpy roads or roads cut by floods; expensive transportation fees, for example, too long or too frequent schedules and appointments with health care providers; long waiting time during hospital visits, poor quality of health care services; and especially low confidence in health care staff including nurses, counselors, physicians (Nakiyemba, 2005). Moreover, a study on barriers to adherence to antiretroviral therapy in Togo indicated that the cost of travel (transportation) and treatment accounts for about 26 and 14 percent, respectively, to be the reasons for poor adherence (Potchoo, Tchamdja, Balogou, Pitche, Guissou, & Kassang, 2010). However, some previous research found that far distance from health care facilities was not significantly associated with poor adherence (Hardon et al., 2006; Cauldbeck et al., 2009).

1.1.2.2.4.5. Predictors related to other factors

There are some other factors associated with poor adherence to ART such as lack of family members, friends, and social support; stigma and discrimination; no reminders or alarm clocks; alcohol as well as injecting drug use; and poor relationship between patients and health care providers. One study on barriers to ART adherence found that a lack of social support was associated with sub-optimal adherence to antiretroviral therapy (Williams & Friedland , 1997). Another study in three countries in Africa, including Botswana, Tanzania, and Uganda, reported that patients complained of lack of social support, felt isolated, abandoned, and even stigmatized from family members, friends, neighbors, and from others. These reasons were the main factors that influenced their poor adherence (Hardon, et al., 2006). Another study revealed that use of alcohol, drugs, and injecting drugs were also linked to sub-optimal adherence (Grierson, Misson, McDonald, Pitts, & O'Brien, 2002).

1.1.2.3. Adherence assessment

Before the era of highly active antiretroviral therapy (HAART), many AIDS patients died, mainly due to opportunistic infections and other related AIDS-related diseases. Since HAART has been developed and given to AIDS patients, however, the number of HIV/AIDS patients dying is substantially decreasing. Moreover, HAART can improve the quality of life and survival of HIV/AIDS patients by reduction of CD4 destruction, HIV viral load in blood, opportunistic infections and other related diseases if patients adhere to ART plans well (Markos, Worku & Davey, 2008). While poor adherence results in the development of HIV drug resistance, ART

failure, decrease in CD4 cell counts as well as low rate of HIV viral load in blood detection, high morbidity and mortality rate, eventually lower ART success.

Adherence to ART is defined as sticking to the treatment plan by taking the correct dose of drugs at the correct time and in the correct way (such as with the right type of food or fluid). It also means looking after drugs to make sure they are safe and effective to use (Castro, 2005).

ART cannot be successful unless adherence is optimal, at least 95 percent. This level is very difficult for HIV/AIDS patients to achieve because it requires high commitment and life-long treatment (Paterson et al, 2000; Castro, 2005).

Adherence measurement is a challenging job for health care providers, especially counselors, in order to identify poor and good adherent patients. It depends on ART regimens, the availability of means of adherence assessment, and it varies from one country to another (developing country to developed country). To achieve ART success, an accurate assessment of adherence is necessary and patients require having at least 95 percent of adherence level (WHO, 2003). Currently, however, there is no gold standard to measure adherence to ART. For that reason, the researchers have developed and classified adherence assessments into two categories. The first category is direct and objective measures such as directly observed treatment, therapeutic drug monitoring, biomarkers, and medication event monitoring system. The second category is indirect measures, which consist of pharmacy records, pill

counts, self-reports, pill identification tests, and VAS (Steel, Nwokike, & Joshi, 2007).

It seems more likely that direct and objective measurement is more accurate and reliable than the indirect measurement of adherence. Despite that, poor resource settings cannot afford to use this measurement because it is more costly and complicated than indirect measurement.

Although self-reporting has been found to overestimate adherence, VAS is still a simpler, cheaper, easier, valid and reliable tool to measure adherence to ART in resource-constrained settings (Walsh, Mandalia, & Gazzard, 2002).

HIV/AIDS patients' counselors at the Infectious Disease Department of Sihanouk Hospital Center of HOPE use both pill count and self-report (VAS) methods to measure adherence (Samnang & Soklida, 2010). Pill count is usually conducted at the hospital by requiring patients to bring their medications when they see counselors on each hospital visit. In order to assess adherence, counselors count the numbers of pills in the bottle and determine whether or not there are any missed doses by comparing the actual number of tablets that physicians have prescribed to patients. Finally, counselors report that patients have optimal (good) adherence if they missed fewer than or equal to three doses per month. In contrast, missing at least four doses in the last month before a patient's visit represents sub-optimal (poor) adherence to ART. Though adherence measurement using pill count is likely to be more accurate than VAS, it still has some disadvantages. For example, patients may

not take their ARVs at home; they instead hide their tablets or throw them away and then they keep only the actual number of tablets needed to be shown to counselors. Additionally, while counselors may have completed the pill count and noted the data on the patients chart, the data are not then entered into a database as VAS is (Samnang & Soklida, 2010).

The Visual Analogue Scale (VAS) method was employed to measure self-reported adherence of patients in the last month prior to their hospital visit by using a 10-centimeter scale, which ranges from 0 cm to 10 cm on a ruler. The counselors ask patients to put a mark somewhere on the ruler and then counselors measure and compute it into percentages; 0 cm, the beginning of the ruler, shows that they have not taken their pills at all, while 10 cm, the end of the ruler, indicates that they have taken all their prescribed pills (Samnang & Soklida, 2010). For the purpose of study and research, the Infectious Disease Department of Sihanouk Hospital Center of HOPE asks counselors to collect VAS data, which have been collected at every patient's visit.

Based on the availability of VAS data in the cohort database of the Department, the author decided to choose VAS as a measurement of adherence and method of data collection on adherence in this study.

1.1.2.4. Previous study findings

As mentioned above, in general, poor adherence to medication is common throughout the world.

It is estimated that around 50% of the world's HIV/AIDS patients have taken their prescribed ART medications inappropriately (Paterson, et al., 2000). Adherence to antiretroviral therapy varies from 37-83% in relation with drugs under study (Steel, Nwokike, & Joshi, 2007). In addition, more than 10% of patients report missing at least one medication dose on a daily basis, while more than 33% report missing doses in the past two to four weeks (Chesney , 2000).

Several studies have presented their adherence findings in developed countries as follows: According to the World Health Organization (2003), the level of adherence to chronic disease treatment was about 50% in the developed countries. One study in the United States of America found that 50 to 60 percent of HIV/AIDS patients failed to reach good adherence (greater than 95%) (Stone & Smith, 2004). The factors for poor adherence in that study were total pills per day, dosing frequency, dietary restrictions, pill size, number of prescription and medication, and bed time dosing. Another example of limited ART adherence of patients in Canada was found in a retrospective study with additional prospective component in which only 75% of patients had greater than 80% adherence to antiretroviral therapy. The reasons for missing doses were forgetfulness, dietary restrictions, inconvenient dosing schedule, and difficulty scheduling administration time around meals (Ostrop, Hallett, & Gill, 2000).

Some studies in the developing countries have found that adherence levels to ART were sub-optimal. The adherence level of one study on adherence to ART in

Brazil was only 75% (95% confidence interval 73.08-76.95). The factors for poor adherence were complex regimens, a large number of pills, illiteracy (under two-year study), and age less than 44 years (Nemes, Carvalho & Souza, 2004). In Africa, a number of studies have shown low levels of ART adherence. For example, the National AIDS and STI Control Program (NASCOP) of Kenya study on a review of records for a 20-month period indicates that 13 percent of the patients had left the area, had discontinued use of ART, or had died (Wanjohi, 2009). Another study estimated that one quarter (25%) of ART users did not achieve optimal adherence (Hardon et al., 2007). Of more concern, a recent systematic review of ART programs reported that about 40 percent of all patients receiving ARVs were thought to have died or discontinued their treatments within two years of treatment.

There were several similar examples of poorer levels of adherence reported by Maria (2008): Studies on ART adherence in urban and rural areas in 2007 by the Catholic Diocese of Ndola, Zambia and Catholic Archdiocese of Mombasa, Kenya found that adherence levels were 60% and 76%, respectively. Also, the Ashar Alo society, Bangladesh found similar adherence levels in rural areas. Moreover, in Bolivia in 2007, the Instituto para el Desarrollo Humano reported that the adherence level studied by a local university was only 50%, which was the primary problem for antiretroviral therapy. In addition, data summarized by the Catholic Relief Service (CRS), from nine countries within their ART program from 2005 to 2007, showed that HIV/AIDS patients still had poor adherence to ART as follows: Kenya 6%,

Zambia 10%, Uganda 12%, and Nigeria 14% (Maria, 2008). The factors that influenced poor adherence in the studies reported by Maria (2008) were multi-faceted, however, they, in general, had similar characteristics including the cost of transportation, laboratory tests, lost wages due to long waiting times, hunger and nutrition, the need for continuous support for patients on treatment, misinformation, side effects, and lifelong antiretroviral therapy.

Also, a survey of 291 AIDS patients in Ethiopia showed that the prevalence of adherence in the week prior to the interview was 74.2%. The factors of non-adherence to antiretroviral therapy were busyness or forgetfulness (51%), change in daily routine (9.4%), and being away from home (8.3%). Moreover, the most common reasons for poor adherence reported by patients were symptoms or side effects in the past four weeks, followed by living more than 47 km away from a health facility (Markos, Worku, & Davey, 2008).

Similarly, a cross-sectional study of 43 patients using the health facilities of the Center for Special Clinic in Sagamu, Nigeria reported that approximately 80 percent of patients reached an adherence level of 95%. The most common reasons for non-adherence was the cost of drugs; however, socio-demographic variables and number of pills taken as well as dosing frequency per day were not significantly associated with poor adherence to antiretroviral therapy (Ogundahunsi, Daniel, & Oladapo, 2008). Poor adherence levels were also found in an evaluation of antiretroviral therapy results of 717 patients who had visited ART clinic in Blantyre,

Malawi. 59% of the total patients were lost to follow-up. Furthermore, during adherence interview, only 92 (52%) patients reported never missing a single dose of medication. The main reasons for loss to follow-up were unavailability of drugs, personal financial problems, and side effects of ART (Oosterhout, et al., 2005). Another example of poor adherence level was shown in a study of knowledge and adherence to antiretroviral therapy among adult people living with HIV/AIDS treated in the health care centers of the association "Espoir Vie Togo" in Togo, West Africa. The study demonstrates that the average adherence rate was about 90 percent, while an adherence rate of greater than or equal to 95 percent was about 63 percent. Poor adherence was mainly due to forgetfulness, followed by travel, cost of treatment, and side effects of drugs; however, gender, age groups, educational levels, and ART drug regimens were not significantly associated with poor adherence (Potchoo, Tchamdja, Balogou, Pitche, Guissou, & Kassang, 2010).

In Asia, sub-optimal (less than 95%) adherence level was also confirmed by the following studies. A study of 60 HIV/AIDS patients on ART in India found that only 60 percent of patients reported that they took their ARVs correctly (Cauldbeck, et al., 2009). Adherence was statistically significantly associated with regular follow-up. Other factors, such as older patients, male gender, side effects, those from larger family, those who had previously AIDS defining illness, those taking fewer medicines and without food restrictions, were not statistically significantly linked to adherence, however, they had a positive trend. In contrast, level of education, family

income, distance from clinic, and time since diagnosis or time on ART had a negative trend away from adherence (Cauldbeck, et al., 2009). In addition, another study on adherence to antiretroviral therapy and virologic suppression among HIV-Infected persons receiving care in private clinics in Mumbai, India found that 73.5% of the total 279 participants reported adherence greater than or equal to 95% in the past four days, 16.1% and 10.4% took 70-94% and less than 70% of their prescribed doses, respectively. The main reasons for poor adherence were running out of pills, traveling away from home, feeling sick or ill, forgetfulness, and being busy with other things. Regimens-related factors significantly correlated with adherence were cost of ART per month, regimen with more than or equal to three antiretroviral drugs, and taking more than or equal to three pills per day. In addition, adherence was positively linked to age older than or equal to 50 years, co-morbid conditions, efficacy of medications, absence of pain in the last month, and support from family and friends. However, lack of reminders to take medications from family or friends, confusion of ART regimens, side effects of drugs, and presence of pain in the last month were negatively associated with adherence (Shah, et al., 2007). Another poor adherence level was also shown by a study on factors associated with adherence to antiretroviral therapy among HIV/AIDS patients in rural China. Of the total 181 participants, 81.8% reported $\geq$ 95% ART adherence on the previous three days. The main causes of missing doses included forgetfulness, being busy, and ART adverse effects. Furthermore, knowledge of patients of ART side effects, belief in the efficacy of ART, reminder tools of taking antiretroviral drugs, and confidence and trust of

patients in their health care providers were independently associated with adherence. While patient's knowledge of ART and socio-demographic factors were not associated with adherence (Wanga & Wu, 2007).

Likewise, several studies in South-East Asian countries have found poor levels of adherence to antiretroviral therapy as mentioned above. Taken as an example, a study on a review of records of all hospitals in Northern Thailand demonstrated that 246 of the 819 AIDS patients had dropped out from health facilities after six months on ART. The main factors for missing doses were side effects of medications, financial constraints, forgetfulness, better health condition, living away from home, being busy with many things, sleeping through dose time, and change in routine (Charukanya, 2008). Another study in Vietnam shows that 37 percent of 151 patients adhered poorly ($< 95\%$) to ART. The reasons for missing doses were forgetfulness, being busy, sleepiness, and stress. Moreover, results of multivariate analysis revealed that ten factors were statistically significantly associated with poor adherence, including the use of alcohol in the last one month, unemployment, use of drugs early or late, no reminders at home, no mention of reminder tools by doctors in the last three months, no counseling on HIV prior to starting ART, no effective support from spouses, fear of being exposed at the clinic, being less interested in the last seven days, and a detectable viral load above 400 copies/mL during interviews. However, socio-demographic factors such as gender, age, and marital status did not affect adherence to antiretroviral therapy (Huong, 2009). In Cambodia, the majority

of HIV/AIDS patients have performed good adherence; however, the remaining patients still have poor adherence levels (< 95%). Figure 1.5 below shows poor levels of ART adherence in three different settings in Cambodia.

Figure 1.5: Poor levels of ART adherence in Cambodia

The graph shows the percentage of poor ART adherence across three settings:
- Nationwide: 13
- Calmette: 29
- SHCH: 3

Y-axis labeled "%" with values 0, 10, 20, 30, 40.

NAA, 2007; AIDS Rsearch and Treatment, 2010 & SHCH 2010
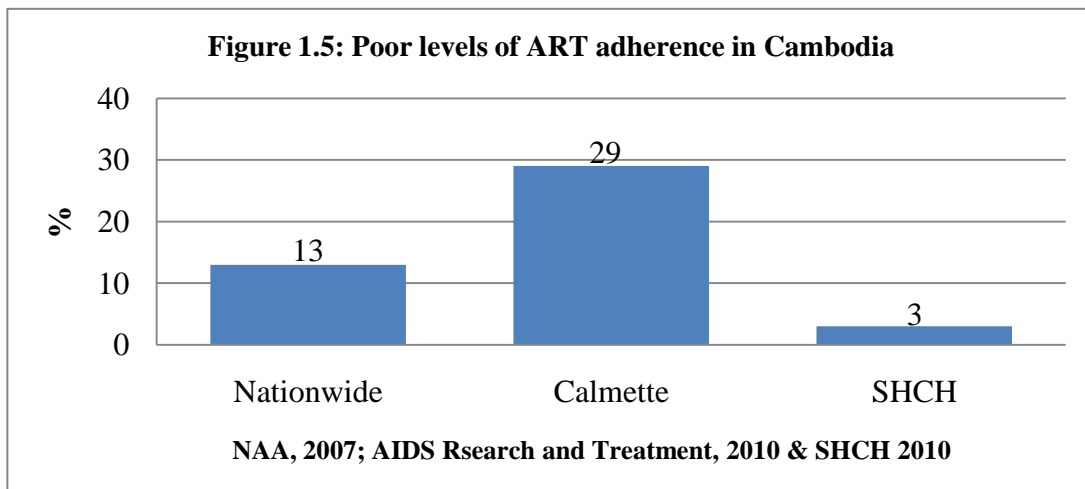
This graph shows that Calmette Hospital has the worst level of ART adherence (29%), while nationwide, 13% of HIV/AIDS patients have poor adherence level. Sihanouk Hospital Center of HOPE (SHCH) has the best level of adherence, with only three percent of patients exhibiting poor adherence.

As mentioned above, universal access to ART has increased substantially in order to meet the demand of HIV/AIDS patients in Cambodia and the rest of the world. To achieve antiretroviral therapy's success, optimal adherence (≥ 95%) to ART must be reached. In fact, HIV/AIDS disease cannot be cured. Hence, it requires lifelong treatment which makes ART adherence a high concern in both developed and developing countries such as Cambodia. There has been so far no research conducted

on barriers to antiretroviral therapy in Cambodia. Therefore, a study on barriers to adherence of HIV/AIDS patients to antiretroviral therapy is needed.

1.2. Research objectives

1.2.1. Main objective

The main objective is to identify barriers, which are associated with poor adherence to ART.

1.2.2. Specific objectives

The specific objectives are:

- To identify if there are any ART side effects associated with poor adherence to ART.

- To identify if there are any ART regimens associated with poor adherence to ART.

- To identify if there are any co-opportunistic infection treatment drugs associated with poor adherence to ART.

- To identify if there are any levels of patient knowledge of ART associated with poor adherence to ART.

- To identify if there are any educational levels of patients associated with poor adherence to ART.

- To identify if patient's location of residence is associated with poor adherence to ART.

- To identify if poverty is associated with poor adherence to ART.

- To identify if there are other socio-demographic and economic factors associated with poor adherence to ART.

1.3. Research questions

In order to meet the objectives above, one main question and eight specific questions were asked as follows:

1.3.1. Main question

What barriers are associated with poor adherence to ART?

1.3.2. Specific questions

- What ART side effects are associated with poor adherence to ART?

- What ART regimens are associated with poor adherence to ART?

- What co-opportunistic infection treatment drugs are associated with adherence to ART?

- What levels of patient knowledge of ART are associated with poor adherence to ART?

- What educational levels of patients are associated with poor adherence to ART?

- Which patient's location of residence is associated with poor adherence to ART?

- What poverty status of patients is associated with poor adherence to ART?

- What other socio-demographic and economic factors are associated with poor adherence to ART?

1.4. Research hypotheses

- ART side effects may influence adherence to ART.

- ART regimens may influence adherence to ART.

- Co-opportunistic infection treatment drugs may influence adherence to ART.

- Levels of patient knowledge of ART may influence adherence to ART.

- Educational levels of patients may influence adherence to ART.

- Patient's location of residence may influence adherence to ART.

- Poverty status of patients may influence adherence to ART.

1.5. Significance of the study

As mentioned above, poor adherence to ART is of high concern in developed and developing countries. By discovering barriers or factors, which are associated with poor adherence to ART in Cambodia and in SHCH, this study can first help practitioners and policy makers to improve the success of their ART program. Second, the study can improve the quality of life of HIV/AIDS patients by reducing burdens of HIV/AIDS disease, HIV drug resistance, ART failure, morbidity and mortality as well as offering them a good opportunity to live normally. Finally, this research is able to contribute to the Cambodian government through saving more money from spending on prevention of HIV transmission, patient care, treatment,

support, and other related managements so that the government can further alleviate the poverty of the Cambodian people as well as increase the opportunities to develop the country.

1.6. Limitations and constraints of the study

First, this study used a self-report method, the Visual Analogue Scale (VAS), which is a subjective tool, to assess patient's adherence to antiretroviral therapy based on available data at the Infectious Disease Department of Sihanouk Hospital Center of HOPE. It may be less accurate than pill count technique, which is objective, to measure adherence, however, there were no available data of pill count at the study site. Second, study subjects were only focused on HIV/AIDS patients. It would be better if health care providers had also been included as the study subjects because they can make research findings more reliable. Third, this study was conducted only in one setting, Sihanouk Hospital Center of HOPE, which seems not to generalize other settings in the entire country.

1.7. Organization of thesis

This research is divided into four main chapters as follows:

Chapter I provides a detailed description of (1) the rationale of the study which includes background of the study, literature review and problem statement, and conceptual framework, (2) research objectives, (3) research questions, (4) research

hypotheses, (5) significance of the study, (6) limitation of the study and (7) organization of thesis.

Chapter II illustrates comprehensive processes in the study, which include study design, sampling methods, methods of data collection, ethical considerations, and data analysis.

Chapter III elaborates on the research findings that are divided into two main parts. First, results are presented in a descriptive analysis embodying socio-demographic and economic characteristics, knowledge of research participants of ART drugs, ART regimens and OI treatments of research participants, ART side effects of research participants, ART adherence characteristics and reasons reported for missing ARV doses in this study. Second, results of association between dependent and independent variable analysis are presented, including results of association between hypothesis testing and adherence to ART analysis and results of association between socio-demographic and economic factors and adherence to ART of analysis.

Chapter IV describes (1) a brief summary of the problem statement; research objectives; research methods, which include study design, sampling methods, methods of data collection, and data analysis (2) discussions which focus on a summary and comparisons of the current research findings with those of previous research in accordance with results of reasons reported for missing ART doses in this study, results of hypothesis testing, and results of socio-demographic and economic

factors, (3) conclusions which are drawn from the main and significant findings of the study, (4) policy implications which involve a comprehensive intervention of improving ART adherence, and (5) finally suggestion for future research that needs to be conducted to fill up the gaps of the current study.

The Next chapter will explain research methods used in conducting this study.

CHAPTER II: RESEARCH METHODOLOGY

2.1. Overview of research methodology

This chapter explains in detail the overall procedures and methods used in the study. The chapter is divided into 13 main parts that include the study design, study area and time frame, target populations, study populations, sample populations, inclusion criteria, exclusion criteria, study variables, sampling procedures, methods of data collection, ethical considerations and administrative formalities, data processing and analyses, and finally a chapter summary.

2.2. Study setting

This study was conducted at Sihanouk Hospital Center of HOPE (SHCH) situated in Phnom Penh, the Capital City of Cambodia, with a population of about one million, the highest population density in the country, and is well known as the economic, public administration, political, education, tradition as well as culture, national and international trade, and entertainment centers. Sihanouk Hospital Center of HOPE has been operating since 1996, with a mission to be a center of excellence not only in providing further education and clinical training of medical professionals from both public and private health sectors in the country but also in providing 24-hour-high quality, free medical care services to the poor, needy, and disadvantaged in Cambodia.

The hospital has technical and administrative departments. The former includes anesthesia, emergency, information technology, laboratory, internal

medicine, medical records, nursing, physical therapy, radiology, hospitality, surgical, telemedicine, pathology, and infectious disease departments while the latter includes finance and procurement, communication and public relations departments.

The Infectious Disease Department has operated since 1997, after the most widespread epidemic of HIV/AIDS occurred in Phnom Penh and other areas of the Royal Kingdom of Cambodia, with financial support from global funds. The department provides treatment of both opportunistic infection (OI) and antiretroviral therapy (ART) services to people living with HIV/AIDS (PLWHA). The number of HIV/AIDS patients on ART, by March 2010 was 2,467, of which 96 percent were on first-line ART (Sopheak, 2010). The majority of PLWHA (62.39%), who came to receive ART services at the hospital, were living in Phnom Penh.

The decision to choose Sihanouk Hospital Center of HOPE as the study site was made because it is the setting where HIV/AIDS patients come to receive ART program services from many different places of Cambodia, which can generalize the characteristics of the HIV/AIDS patients of the whole country. Moreover, the author used to work there for four years such that he is familiar with the hospital management system as well as hospital staff and patients so that he had easy access to conducting the study.

2.3. Study design and time frame

A comparative cross-sectional survey in the form of a case-control study of poor ART adherent patients as cases against a control group of good ART adherent

patients was conducted at Sihanouk Hospital Center of HOPE from August 16 to September 30, 2010. This research embodies both a quantitative and qualitative perspective in order to provide high quality results based on close-ended questions and open-ended questions in the questionnaire. The close-ended questions involve numbers, which represent a quantitative research perspective, while open-ended questions provide a qualitative research perspective, which seeks for reasons expressed in words behind any study problems.

2.4. Research subjects

2.4.1. Target population

The target population was all HIV/AIDS patients at SHCH.

2.4.2. Study population

The study population was all HIV/AIDS patients who were on ART at Sihanouk Hospital Center of HOPE, Phnom Penh, Cambodia.

2.4.3. Sample population

The sample population consists of 60 poor ART adherent patients and 57 good ART adherent patients. Among the sample population, females represent the majority, 61.5 percent, because more female than male patients had received ART at the hospital.

2.4.4. Inclusion criteria

The inclusion criteria of the research subjects include adult (equal to or older than 15 years old) HIV/AIDS patients who were at least six months on ART, with informed consent signed and agreed to participate in the study.

2.4.5. Exclusion criteria

The exclusion criteria of the research subjects include:

- HIV/AIDS patients who were on ART less than six months

- HIV/AIDS patients who were younger than 15 years old.

- HIV/AIDS patients who had not started ART.

- HIV/AIDS patients who had had mental problems and had been seriously sick.

2.5. Study variables

Study variables are divided into two categories: the dependent variable and independent variables.

- The dependent variable is adherence to ART of the HIV/AIDS patients which could be either poor or good.

- Independent variables consist of attributes that may lead to either poor or good ART adherence which are those listed in the table below.

Independent variables

Table 2.1: List of studied independent variables

Hypothesis testing	Variables
	ART side effects
	ART regimens
	OI drug uses
	Knowledge of ART
	Educational levels
	Patient's location of residence
	Poverty
Socio-demographic and economic factors	**Variables**
	Gender
	Age groups
	CD4 groups
	WHO stages
	Marital status
	Occupations
	Food

2.6. Sampling procedures and methods

2.6.1. Sampling technique

There are two major sampling methods in social science. These are non-probability and probability sampling. The non-probability sampling represents any techniques in which sample selection is not based on the probability theory. Some examples of non-probability sampling are purposive, snowball, and quota sampling

(Babbie, 2005). Probability sampling, however, is any techniques whose sample selections are based on the probability theory. It typically involves some random selection mechanisms such as simple random sampling, systematic random sampling, and stratified random sampling (Babbie, 2005).

The objectives of social research, mainly, are to generalize research findings from the study sample to the larger population and to avoid biases. For that reason, the availability of population as well as precise statistical predictions is very crucial (Babbie, 2005).

Purposive and simple random samplings were used in this study for two reasons. First, purposive sampling was employed based on a small number of poor adherent patients identified under ART program from its beginning to March 2010 at Sihanouk Hospital Center of HOPE. Second, simple random sampling (SRS) was used among good adherent patients whose numbers are much larger than those of poor adherent patients. Moreover, SRS is the probability sampling that can reduce the bias of sample selection since it can provide each research respondent with an equal chance of being selected for the study.

Prior to the interview, the author had discussed with counselors and medical recorders (clerks) the tactic to capture patients, who were to be included in the study, after receiving a list of patient names. First, counselors singled out all patients easily because they have worked at the Infectious Disease Department of Sihanouk Hospital Center of HOPE for many years and their responsibilities were to counsel with

HIV/AIDS patients every day. Second, clerks had put an alarm signal on any patient's computer records if that patient had been shortlisted for interview so as to double check and capture comprehensively all the names of patients.

2.6.2. Sample size

Since the Infectious Disease Department of Sihanouk Hospital Center of HOPE has operated until March 2010, the total number of HIV/AIDS patients under ART program was 2,417, of which 74 (3%) represented patients with poor adherence to ART (Sopheak, 2010).

Based on a small number of poor adherent patients, the author chose to use purposive sampling in a bid to have a bigger sample out of these poor adherent patients. As a result, 60 poor adherent patients were identified. The remaining poor adherent patients had not participated in the study because of inability to contact with them; others lived far away from the research site or just recently had the appointment with physicians prior to the interview.

Simple random sampling was used to select samples from good adherent patients who came to visit the hospital to receive ART, following their appointments with physicians. The number of good adherent patients, who came to see doctors every day, on average, was about 70-100. The simple random sampling was conducted every day among good adherent patients, by putting their names in a hat, then shaking the hat, and picking up a number of lotteries of patients' names from the

hat in terms of required number of the patients for the author. After SRS ended, 57 samples of good adherent patients were selected.

As the research design is a comparative cross-sectional in the form of case-control study, a group of 60 patients who had shown poor adherence was compared with a control group of 57 random patients with good adherence to ART. Therefore, 117 HIV/AIDS patients are included in the study.

2.7. Methods of data collections

Both quantitative and qualitative approaches were used to collect data in this study. In general, there was a variety of techniques used to collect data such as tests and measurements, observations, surveys, documents, and interviews that can help the author reach the objectives of the study (Glatthorn & Joyner, 1993). A face-to-face interview followed a structured questionnaire, as well as both primary and secondary data collection methods was used to conduct this research.

2.7.1. Primary data collection

All eligible respondents who met the inclusion criteria and signed the informed consent were included in the study. The primary data were obtained by face-to-face interviewing of both poor and good ART adherent patients, followed by a self-administered and structured questionnaire to answer research questions.

2.7.2. Secondary data collection

The secondary data used in the literature review and analysis were collected from the database cohort of the Infectious Disease Department of Sihanouk Hospital Center of HOPE, annual reports, monitoring and planning, research, and documents of the National Center for HIV/AIDS, Dermatology, and STD (NCHADS), UNAIDS, WHO, United Nations Children's Fund (UNICEF), and other related research of both local and international institutions.

2.7.3. Data collection on adherence to ART

Figure 2.1: Data collection on ART adherence at SHCH by March 2010
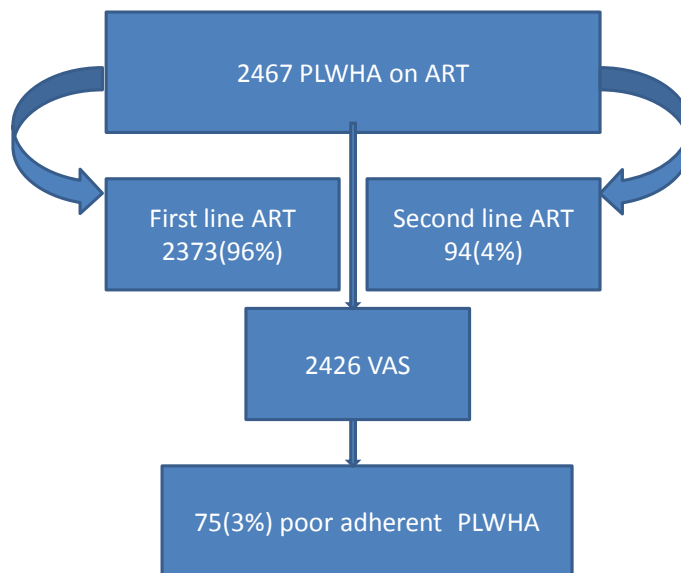
Source: **Infectious Disease Department Database**

At the Infectious Disease Department of Sihanouk Hospital Center of HOPE since the beginning of the program started from 1997 to March 2010, there were 2,467 patients on ART. Of these patients, 96 percent were on first-line ART, while four percent were on second-line ART. However, out of the total 2,467 patients, only 2,426 VAS were conducted, of which three percent were poor adherent patients, while the rest, 97 percent, was good adherent patients. For more detail on VAS, please see adherence assessment in Chapter I.

2.7.4. Research instruments

As mentioned above in this section, there is a variety of tools used to collect data in social sciences. A face-to-face interview, followed by a structured questionnaire through a pre-test questionnaire and a pilot study, was conducted in the study of barriers to adherence of HIV/AIDS patients to antiretroviral therapy at Sihanouk Hospital Center of HOPE, Phnom Penh, Cambodia.

2.7.4.1. Structured questionnaire

A self-administered and structured questionnaire, with both closed and open-ended questions, was designed in this study by using four previous studies. The first study was factors that influence non-adherence to antiretroviral therapy among HIV and AIDS patients in central province, Kenya (NYAMBURA, 2009). The second study was an evaluation of determinants of adherence to antiretroviral therapy in AIDS patients in Gert Sibande District, Mpumalanga Province (Laszchenov, 2009) . The third study was adherence to ART in PLWHA at Yirgalem Hospital, South

Ethiopia (Endrias, Alemayehu, & Gail, 2008). The last study was adherence to antiretroviral therapy among HIV patients in Bangalore, India (Mary et al., 2009). Next, the questions used in the two studies above were adjusted and combined together in order to develop a synthesized as well as reliable questionnaire in this study. The structured questionnaire can provide data, which are objective, scientific, precise, and reliable for hypothesis testing (Ong, 1993).

The questionnaire consists of five main sections: socio-demographic and economic characteristics, knowledge of ART drugs, ART regimens and OI drug treatments, ART side effects, and characteristics of ART adherence and reasons reported for missing ART doses.

The first section, socio-demographic and economic characteristics, focuses on gender, age groups, CD4 groups, WHO stages, marital status, education background, occupation, income, patient's location of residence, and poverty as well as food access status.

The second section, knowledge of ART, is comprised of six questions such as why do you take ARV drugs? How many ARV drugs need to be taken together for effective treatment? How long is the ARV treatment? What are the side effects that may happen during ART? What will you do if side effects happen? The last question, what are the benefits of taking ARVs regularly, continuously, and correctly?

The third section, ART regimens and OI drug treatment, was made up of three questions, including what ART regimen are you currently on? What other drugs

besides ARVs are you currently on? The last question, do you have difficulty taking ARVs while using OI drugs?

The fourth section, ART side effects, has three questions including did you experience ART side effects? What are the side effects that you experienced? Did side effects cause you to stop taking ARVs?

The last section, factors influencing adherence to ART, consists of four questions: do you take ARVs regularly, continuously, and correctly? What are the factors that help you take ARVs correctly? What causes you not to take your tablets? Last question, many people find it difficult to take every single dose of ART; in the last month (prior to the interview date), how many doses did you miss?

2.7.4.2. Pre-test questionnaire and pilot study

Furthermore, a pilot study was conducted with five HIV/AIDS patients from each group (poor and good adherent group) on August 2, 2010, two weeks prior to the interview date. These ten patients were not included in the study in order to avoid any biases, which may occur in the research. Before the pilot study was undertaken, a pre-test questionnaire was translated into Khmer, the local language, and then it was sent to a colleague who has many years of experience working with HIV/AIDS patients and currently is a clinical supervisor at the Infectious Disease Department of Sihanouk Hospital Center of HOPE, which is the research site. Therefore, the colleague is familiar with the Infectious Disease Department flow, management, and the interview process.

There are four purposes of conducting the pilot study. First is to test the questionnaire whether it makes sense and is easily understandable or not for research respondents. Second is to measure how long it takes for conducting the interview. Third is to adjust as well as modify words, sentence structures, any other grammatical mistakes, questions, and the entire questionnaire. Last is to learn, understand, pre-examine, and to predict what would happen during the process of actual field research.

After the pilot study was conducted, some words, written expressions, sentence structures, questions, and answers of the questionnaire were edited and changed to make them simple, precise, and more comprehensive to the research subjects.

2.7.4.3. Interview with patients having poor and good adherence to ART

Interview is one of the main methods used to collect data in many kinds of research. It consists of several forms such as face-to-face interview, focus group discussion interview, and telephone interview. The face-to-face interview through a self-administered and structured questionnaire, without exception, was employed to collect data in this study. There are four reasons to choose this interview approach. First, there is a limitation of research respondents' knowledge to fill up the questionnaire since the majority of Cambodian people have low literacy rate, especially those from the countryside and HIV/AIDS patients. Second, the author can have the best opportunity to explain and clarify in detail both any doubts or questions

from the respondents and questions, answers as well as contents in the questionnaire. Third, the interview can allow the author to receive a high response rate from respondents. It is more likely that while staying and talking together with the interviewer, respondents are able to answer questions and fill up the questionnaire. Last, the author, at the same time, can play two roles in both interviewing respondents and observing their behavior directly. Hence, the interviewer can learn and better understand the situation of interviewees that may occur during the interview.

Furthermore, the interview section is divided into two parts: interviewer and interview process.

2.7.4.3.1. Interviewer (the author)

The interviewer used to work with HIV/AIDS patients at the Infectious Disease Department of Sihanouk Hospital Center of HOPE for four years. For that reason, he has plenty of experiences providing voluntary confidential counseling and testing (VCCT), treatments as well as care services, and other related managements to HIV/AIDS patients. Therefore, he is not only familiar with the flows and management system of the hospital but he also knows most of the patients who came to receive ART service program. Eventually, the author was able to interview study subjects with high response as he expected.

2.7.4.3.2. Interview process

Before going to Cambodia, the author has received official permission letters from the Head of the Infectious Disease Department and director of Sihanouk

Hospital Center of HOPE and from the National Ethics Committee for Health Research of the Ministry of Health of Cambodia. After arriving in Cambodia, the author contacted the Head of the Infectious Disease Department of the hospital in order to discuss the interview and field research process with respondents. After a detailed and thorough discussion, the Head of the Department assigned a counselor to facilitate the interview since the counselor is responsible for working and counseling with patients every day. Hence, he is very familiar with respondents.

Most of the respondents had appointments with physicians during the interview period; however, some respondents had their appointments before and after that period. In order to get enough sample size for the study, the author needed to contact, telephone, and make an appointment with those respondents whose follow-ups were not in the period of study before the interviews took place.

With full support and good cooperation from the Infectious Disease Department's staff, including the Head of the Department, Head of the Department assistant, database manager, physicians, counselors, medical recorders, and nurses, the interviews with poor and good adherent patients on ART were conducted smoothly and lasted 45 days starting from August 16 to September 30, 2010 in a separate, private, and confidential room at the Infectious Disease Department of Sihanouk Hospital Center of HOPE.

At the beginning of the interviews, the author provided a self-introduction, clear and detailed explanation of the topic as well as purposes of the study, the

duration of the interview, and informed consent to survey subjects. Also, the author had made them aware that they could choose to participate in or to quit the interview at any time if they did not want to answer questions. Having fully understood the overall content of the study, all 117 respondents accepted and agreed to sign the consent form. Therefore, 117 HIV/AIDS patients were included as a survey sample in this study.

The author conducted face-to-face interviews through a self-administered and structured questionnaire with all respondents who were included in this study. On average, the interview with each respondent took approximately 20-30 minutes in order to obtain detailed information. However, it took a longer time with respondents who had a low level of knowledge and difficulty in understanding questions and answering questionnaire. In fact, the interviews with respondents were conducted with full respect and regard to ethical considerations and administrative formalities.

2.8. Administrative formalities and ethical considerations

This section is divided into two parts: administrative formalities and ethical considerations.

2.8.1. Administrative considerations

In Japan, the request letter to do field research in Cambodia was approved by the author's supervisor, GHOTBI Nader, and the academic office of Ritsumeikan Asia Pacific University (APU).

Moreover, the author had written and submitted necessary documents to the Infectious Disease Department of Sihanouk Hospital Center of HOPE as follows:

- The author's request letter to Dr. Thai Sopheak, Head of the Infectious Disease Department of Sihanouk Hospital Center of HOPE and Mr. Kevin O' Brien, Executive Director of Sihanouk Hospital Center of HOPE

- Recommendation letter from the supervisor of Public Health Management Program of APU to Sihanouk Hospital Center of HOPE to conduct field research (appendix 3)

- Summary of the study protocol in English and in Khmer

- Detailed study protocol in English

- Questionnaire in English and in Khmer

- Consent form in English and in Khmer

Also, the following compulsory documents were written and submitted to His Excellency Professor ENG Huot, Chairman of the National Ethics Committee for Health Research of the Ministry of Health of Cambodia.

- The author's request letter for conducting field research at Sihanouk Hospital Center of HOPE

- Recommendation letter from the supervisor of Public Health Management Program of APU to National Ethics Committee for Health Research of Cambodia to conduct field research (appendix 4)

- Cover letter on submission of study protocol to the National Ethics Committee for review

- Application form

- Summary of the study protocol in English and in Khmer

- Detailed study protocol

- Questionnaire in English (appendix 2) and in Khmer

- Consent form in English (appendix 1) and in Khmer

- Permission letter from Sihanouk Hospital Center of HOPE   (appendix 5)

- The author's CV

In Cambodia at Sihanouk Hospital Center of HOPE, Dr. Thai Sopheak, Head of the Infectious Disease Department and Mr. Kevin O' Brien, Executive Director of Hospital approved the author's request and permitted him to conduct field study at the Hospital. Furthermore, His Excellency Professor ENG Huot, Chairman of National Ethics Committee for Health Research of the Ministry of Health of Cambodia also approved the author's request and proposal to do field research at Sihanouk Hospital Center of HOPE. Finally, the permission letter for conducting field research was authorized by the President of National Ethics Committee for Health Research of Cambodia (appendix 6).

2.8.2. Ethical considerations

Ethical conduct is one of the key elements of the entire research process that needs to be maintained throughout the study. Every effort to protect the health and rights of the research subjects must be made (World Health Organization, 2004) .

In order to adhere to the ethical conduct for health research, in this study informed consent was sought from the study population during the field data collection because HIV/AIDS is one of the most sensitive issues in medical research. Therefore, anonymity and confidentiality of the study subjects must be guaranteed. For this reason, a number of measures were taken:

- No names and other related information of all study subjects were recorded in the questionnaire or other documents.

- The privacy of all study subjects was protected during the interview session.

- The subjects had the rights to refuse or withdraw if they do not want to be included in study sample.

- The participation of the study subjects was voluntary.

- The information and data collected in the questionnaire from the interviews have been kept in safe manner and will be destroyed after data have been entered, double checked, and analysis.

- Nobody can access the study subjects' information, except for the author.

- No money or any forms of goods were provided to research respondents in order to avoid any biases of the study.

At the end of the interview, every research subject would receive words of appreciation and gratitude as well as a final assurance of anonymity and confidentiality from the author.

2.9. Data analysis

This section is classified into four main parts. The first part is data organization, management, displays, and statistical package SPSS analysis. The second part is descriptive data analyses. The third part is hypothesis testing and Chi-square test for association analyses. The last part is socio-demographic and economic factors and Chi-square test for association analyses. For further detail of each part, please see its descriptions and explanations as follows:

2.9.1. Data organization, management, and displays using statistical package SPSS analysis

This section explains the procedure by which data for statistical analysis were constructed. The procedure of converting the original responses in the survey to the variables (data) used in the statistical analysis consists of five steps. First, the questionnaire used in the interviews was written in Khmer (local language) in order for the research respondents to easily understand the overall meanings and contents of the questionnaire. Second, after the questionnaire was successfully completed, the author double-checked the answered questionnaire before translating it into English.

Third, all data in the questionnaire were coded, sorted, and grouped according to the study variables and purposes of the author's study after they were entered into Microsoft Excel file, cross-checked, inspected, and scrutinized so as to ensure accuracy, relevance, completeness, consistency, and uniformity of collected data.

Fourth, after the data in Microsoft Excel file were carefully and thoroughly cleaned, they were transported into statistical package SPSS file. Finally, data were again coded, sorted, and grouped into a concrete and precise organization before they were analyzed using Statistical Package SPSS software version 18.

2.9.2. Descriptive data analysis

Descriptive data analysis provides basic information, overall features, and characteristics of research respondents in the study. The descriptive data analyses mainly focus on five major parts.

First data analysis involves socio-demographic and economic characteristics of research respondents, which focus on gender, age groups, CD4 groups, WHO stages, marital status, educational levels, occupations, patient's location of residence, and economic and food access status of research respondents.

Second data analysis focuses on knowledge of research respondents on ART, which concentrates on assessing their knowledge, and understanding of the overall benefits and contents of antiretroviral therapy (ART). Six questions were asked in order to assess knowledge of ART, which include why do you take ARV drugs? How many ARV drugs need to be taken together for effective treatment? How long is the

65

ARV treatment? What are the side effects that may happen during ART? What will you do if side effects happen? And the last question was, what are the benefits of taking ARVs regularly, continuously, and correctly?

Third data analysis encompasses ART regimens, OI drug treatments, which centers on ART regimens and OI drug treatments that research respondents had taken, and also on any difficulties that could occur while concomitantly using these two treatments. Additionally, three main questions were asked to research respondents: what ART drugs are you currently on? What other drugs besides ARVs are you currently on? The last question was, do you have difficulty taking ARVs while using OI drugs?

Fourth data analysis focuses on ART side effects that look for any side effects of ART that may have a relationship with adherence to ART. For that reason, three questions were asked: did you experience ART side effects? What are the side effects that you experienced? Did side effects cause you to stop taking your medicines?

Last data analysis involves ART adherence characteristics and reasons reported for missing ARV doses in this study, which focus on seeking any factors that may affect adherence of the HIV/AIDS patients while taking ARVs. In order to determine these factors, four questions were asked: Do you take ARVs regularly and correctly? What are the factors that help you take ARVs regularly and correctly? What causes you not to take your tablets? Many people find it difficult to take every single dose; in the last month, how many doses have you missed?

Moreover, several methods of reporting data in these analyses are included such as raw data, frequency, and percentages. Finally, data are displayed using charts, graphs, tables, figure, and others.

2.9.3. Hypothesis testing and Chi-square test for association analysis

In order to understand this section, the definition of hypothesis and hypothesis testing is given. Lang and Secic (Lang & Secic, 1997, p. 261) state that:

"Hypothesis is a statement that will be accepted or rejected on the basis of the results of the study, while hypothesis testing is a mathematical process of testing a hypothesis on the basis of evidence (data)."

Since the objective of this study is to find out barriers to antiretroviral therapy (ART) adherence of HIV/AIDS patients at Sihanouk Hospital Center of HOPE, Phnom Penh, Cambodia, therefore, the dependent variable is adherence status to ART (poor and good adherence) and the independent variables include ART side effects, ART regimens, OI drug treatments, knowledge of ART, educational levels, patient's location of residence, and poverty status (poor and not poor).

Both dependent and independent variables in this study are categorical variables. The dependent variable is dichotomous (poor adherence and good adherence), while the independent variables are nominal variables. Chi-square test is used to assess relationships between two categorical variables (Godfrey, 1997) after cross-tabulation was done. In this study, the level of significance test used was 5%

(alpha level=0.05). Hence, a P-value less than 0.05 shows a statistically significant association between two categorical variables.

Seven hypotheses were tested in this study:

- ART side effects can influence adherence to ART.

- ART regimens can influence adherence to ART.

- OI drug treatments can influence adherence to ART.

- Knowledge of ART can influence adherence to ART.

- Educational levels can influence adherence to ART.

- Patient's location of residence can influence adherence to ART.

- Poverty can influence adherence to ART.

In these analyses, methods of reporting data are raw data, frequency, and percentages. Then, data are displayed using figures, cross-tabulations, and contingency tables.

2.9.4. Socio-demographic and economic factors and Chi-square test for association analysis

The Socio-demographic and economic factors apart from those tested in hypotheses above were also assessed by Chi-square test for association analysis in order to identify any relationships with adherence to ART. These factors were gender, age groups, CD4 groups, WHO stages, marital status, occupations, and food access status.

In these analyses, methods of reporting data are raw data, frequency, figures, and cross-tabulations.

2.10. Chapter summary

This chapter explained detailed procedures of the survey. It describes three steps of field research. First, how the questionnaire was designed, developed, and checked in a pilot study before the field research was conducted. Second, how the study sample was selected as well as how the interviews and methods of data collections were decided during the field research process. Finally, the chapter elaborated on data management and analyses using statistical software SPSS after the research field was done.

The next chapter presents the results obtained with those methods.

CHAPTER III: RESEARCH FINDINGS

3.1. Overview of research findings

The results and data interpretations are presented in this section. The findings section is divided into two main parts. The first part is descriptive statistics results that consist of five sub-major parts including socio-demographic and economic characteristics, knowledge of research participants on ART, ART regimens and OI drug treatments, ART side effects of research participants, and ART adherence characteristics and reasons reported for missing ARV doses. The second part is statistically analyzed results of a test for association between two categorical variables that comprises hypothesis testing, and socio-demographic and economic factors. Moreover, hypothesis testing includes results of association using Chi-square test between ART side effects and adherence to ART, ART regimens and adherence to ART, OI drug regimens and adherence to ART, Knowledge of research respondents on ART and adherence to ART, educational levels and adherence to ART, patient's location of residence and adherence to ART, and finally between poverty and adherence to ART.

3.2. Results of descriptive analysis

3.2.1. Socio-demographic and economic characteristics

A survey of 117 HIV/AIDS patients, who had been at least six months on ART, was conducted at Sihanouk Hospital Center of HOPE (SHCH), Phnom Penh,

Cambodia. Of the 117 sample, 60 patients showed poor adherence and 57 patients good adherence to ART.

3.2.1.1. Gender of research participants

Figure 3.1. Gender of research participants
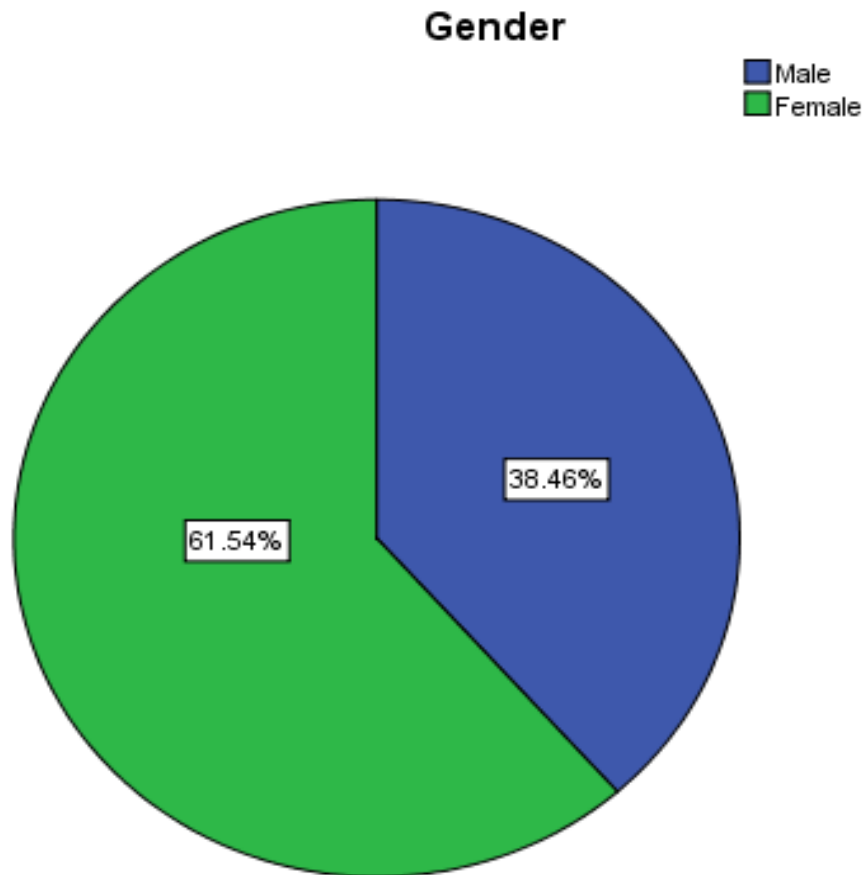
This pie chart shows that the majority of all research participants, 61.5 percent, were females, while the remaining 38.5 percent were males. The males are

believed to be the main cause of transmitting HIV to females through heterosexual relations, especially from husband to wife at the household level.

3.2.1.2. Age groups of research participants

Figure 3.2: Age groups of research participants
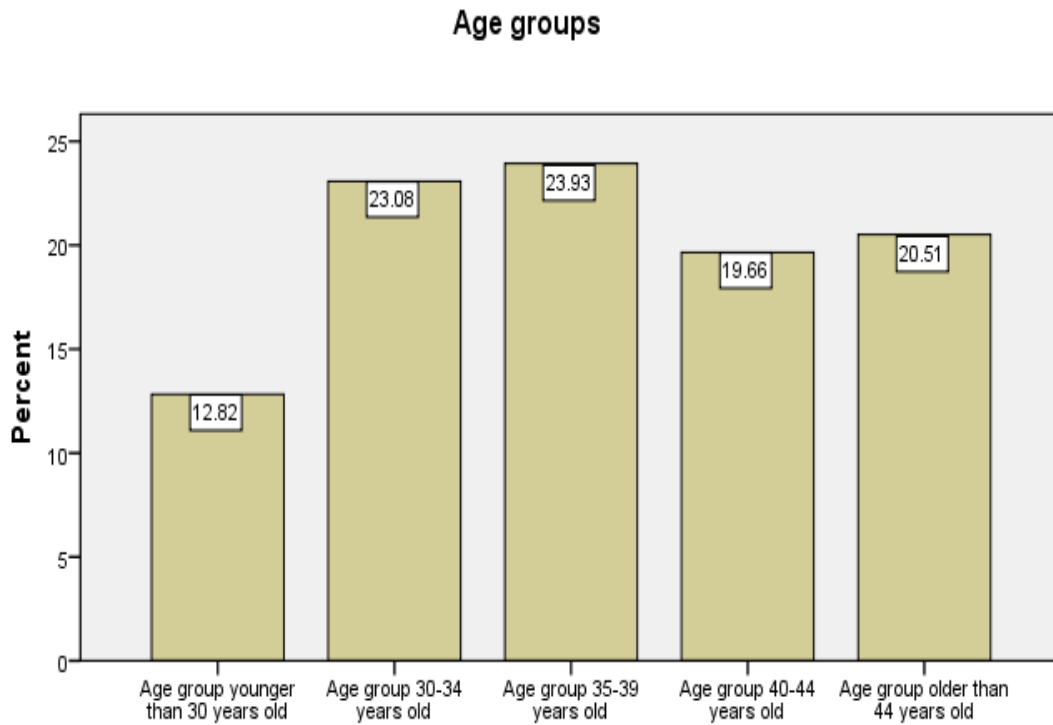
Age groups

This graph shows that age groups 30-34 and 35-39 years old accounted for about 23 and 24 percent, respectively. While age groups 40-44 and older than 44 years old were almost the same, about 20 percent. The age group younger than 30 years old, however, was the smallest one, about 13 percent.

3.2.1.3. CD4 groups of research participants

Table 3.1: CD4 groups

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	CD4 group 1-99	66	56.4	56.4	56.4
	CD4 group 100-199	22	18.8	18.8	75.2
	CD4 greater than 199	29	24.8	24.8	100.0
	Total	117	100.0	100.0	

This table reveals that CD4 group 1-99 accounted for the majority, about 56 percent, while CD4 group 100-199 belonged to approximately 19 percent. These CD4 groups prove that most of the HIV/AIDS patients have very weak immunity that makes them vulnerable to opportunistic infections. The CD4 group greater than 199 accounted for about 25 percent. Patients, who have higher CD4, are most likely to have better protection from opportunistic infections.

3.2.1.4. WHO stages

Figure 3.3 illustrates that about 44 and 35 percent of HIV/AIDS patients, who were on ART, belonged to the seriousness of disease WHO stages 3 and stage 4 respectively, while stage-1 patients accounted for only 6 percent. This shows that patients start ART when the severity of the disease has already increased.

Figure 3.3: WHO stages of research participants

WHO stage

- WHO stage 1
- WHO stage 2
- WHO stage 3
- WHO stage 4

5.98%

14.53%

35.04%

44.44%
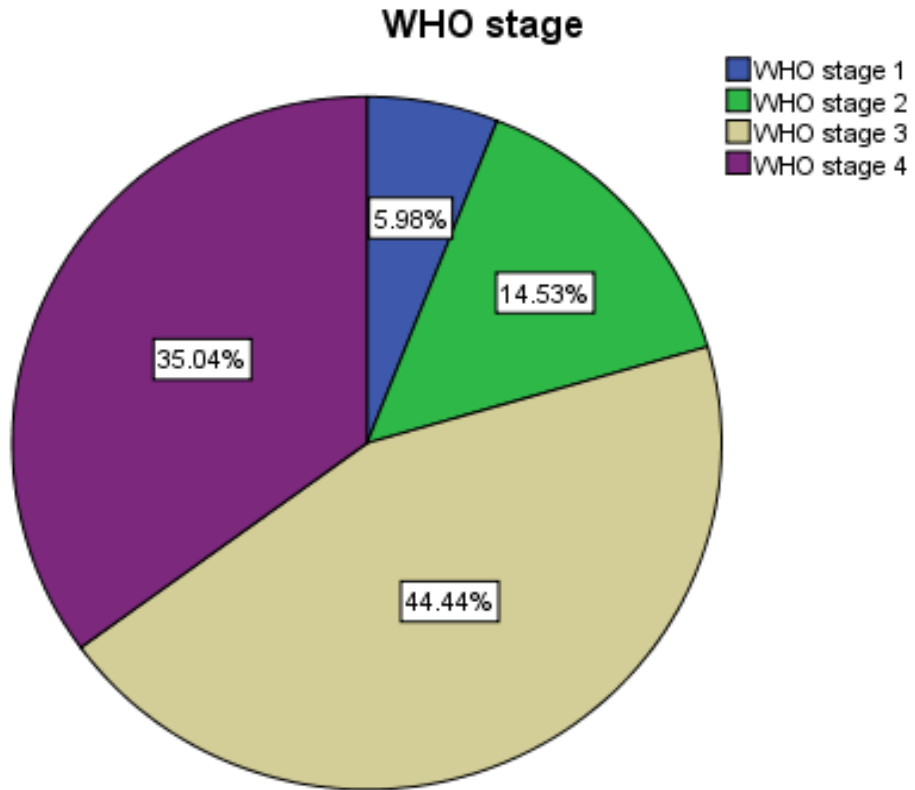
3.2.1.5. Marital status of research participants

Table 3.2: Marital status of research participants

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Single	8	6.8	6.8	6.8
	Married	69	59.0	59.0	65.8
	Divorced	24	20.5	20.5	86.3
	Others	16	13.7	13.7	100.0
	Total	117	100.0	100.0	

This table indicates that most of the respondents (59 percent) were married, whereas 20.5 percent were divorced. The remaining marital statuses such as widowed and co-habiting patients accounted for 13.7 percent.

3.2.1.6. Educational background of research participants

Figure 3.4: Educational level of Research Participants
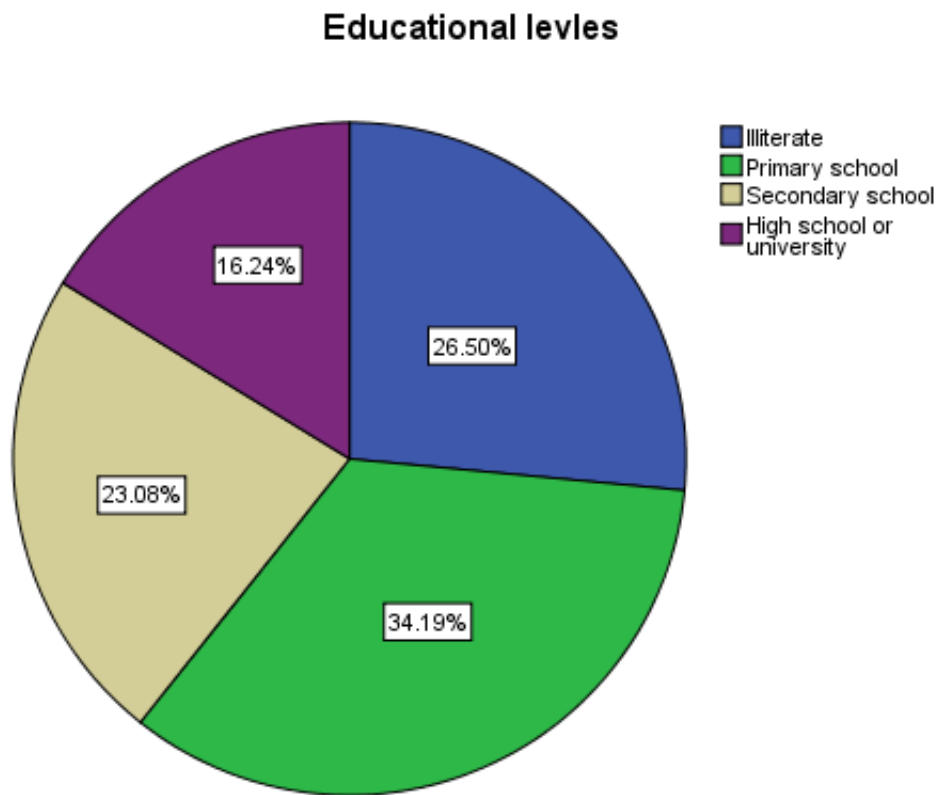
This pie chart demonstrates that about 26 percent of the total research respondents were illiterate, who cannot read and write at all. About 34 percent of the patients had attended primary school, while about 23 percent had studied at secondary school. Attending high school or university, however, accounted for only about 16

percent. Moreover, the trend of studying at higher institutions was decreasing. In general, the educational level of the patients is still limited.

3.2.1.7. Occupation of Research Participants

Figure 3.5: Occupation of research participants

This bar chart indicates that, of all patients, 26 percent were operating small businesses or self-employed, while unemployed and company workers accounted for about 23 and 21 percent, respectively. Other categories such as NGO staff, restaurant and construction workers, and motor taxi drivers accounted for 12 percent.

3.2.1.8. Location of residence of research participants

Figure 3.6: Patient's location of residence
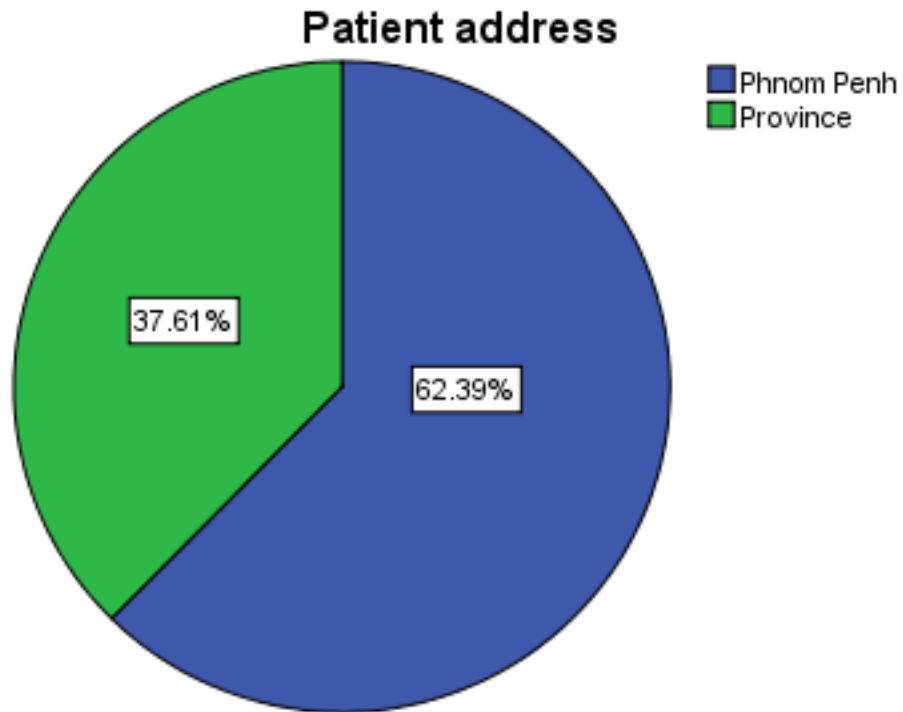
This pie chart shows that most of patients (62 percent) lived in the Capital City, Phnom Penh, where the research facility is situated, while the remaining, 38 percent, lived in provinces, which is more than 30 kilometers away from the research site. Currently, the number of Cambodian people moving from countryside and provinces to live in Phnom Penh is increasing due to lack of jobs in the rural areas.

3.2.1.9. Economic and food status of research participants

Table 3.3: Economic status

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Poor	82	70.1	70.1	70.1
	Not poor	35	29.9	29.9	100.0
	Total	117	100.0	100.0	

Table 3.4: Food access status

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Enough	68	58.1	58.1	58.1
	Not enough	49	41.9	41.9	100.0
	Total	117	100.0	100.0	

Table 3.3 shows that the majority of the patients, 70 percent, were very poor, earning less than 1US$ (1US$=4000 Riel, local currency) per day.

Table 3.4 reveals that 42 percent of the total participants did not have enough food to eat every day, which is higher than the poverty rate in Cambodia. It shows that there is an urgent need for food provision and financial support to the patients.

3.2.2. Knowledge of research participants of ART drugs

To assess the knowledge of ART drugs among the patients, the author provided a score to each question answered by the participants in the knowledge of ART drug section. There are in total six questions in the section. Then, the total score of all answers to the six questions was summed up. Knowledge of ART drugs was divided into two parts. The first part is low knowledge, score equal to or less than 14 and the second part is high knowledge, score equal to or more than 15.

Six questions were asked to investigate whether the patients know about ART or not. Most of the patients had good knowledge of ART.

3.2.2.1. Why do you take ART drugs?

Figure 3.7: Purposes of taking ARVs
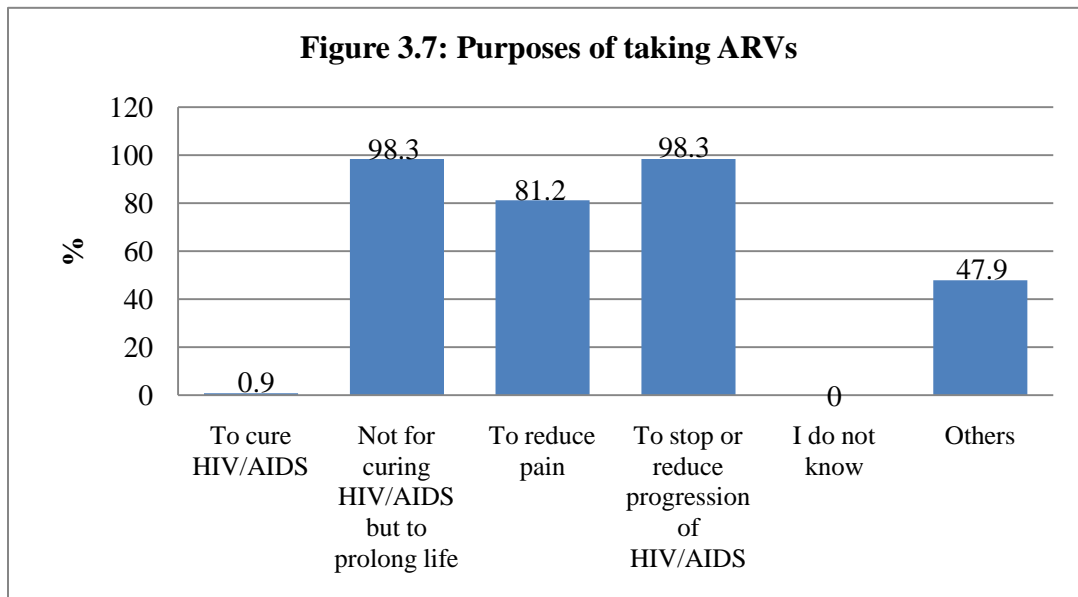
Figure 3.7 demonstrates that almost all patients (98.3 percent) responded that they took ARVs not for curing HIV/AIDS but for prolonging life or for stopping the progression of HIV/AIDS. Only one patient of the samples said he took ARVs to cure HIV/AIDS. In addition, 81.2 percent said they took ARVs to reduce pain. The answer as "others" accounted for about 50 percent, which represents mostly good health, followed by increase in CD4, reduction of HIV viral load in the blood as well as HIV transmission, prevention of opportunistic infections, and prevention of mother-to-child transmission of HIV (PMTCT).

3.2.2.2. How many ARV drugs need to be taken together for effective treatment?

Table 3.5: ARV drugs need to be taken together for effective treatment

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	One ART drug	11	9.4	9.4	9.4
	Two ART drugs	12	10.3	10.3	19.7
	Three ART drugs	93	79.5	79.5	99.1
	Others	1	0.9	0.9	100.0
	Total	117	100.0	100.0	

This table illustrates that about 80 percent of the patients responded with the right answers, saying that they need three ART drugs. The remaining 20 percent of the patients, however, provided wrong answers.

3.2.2.3. How long is the ARV treatment?

Table 3.6: ARV treatment duration

	Frequency	Percent	Valid Percent	Cumulative Percent
Valid Lifelong	117	100.0	100.0	100.0

Strikingly, all interviewed patients said that ARV treatment is lifelong, which is the correct answer.

3.2.2.4. What are the side effects that may happen during ART?

Figure 3.8: Side effects that may happen during ART
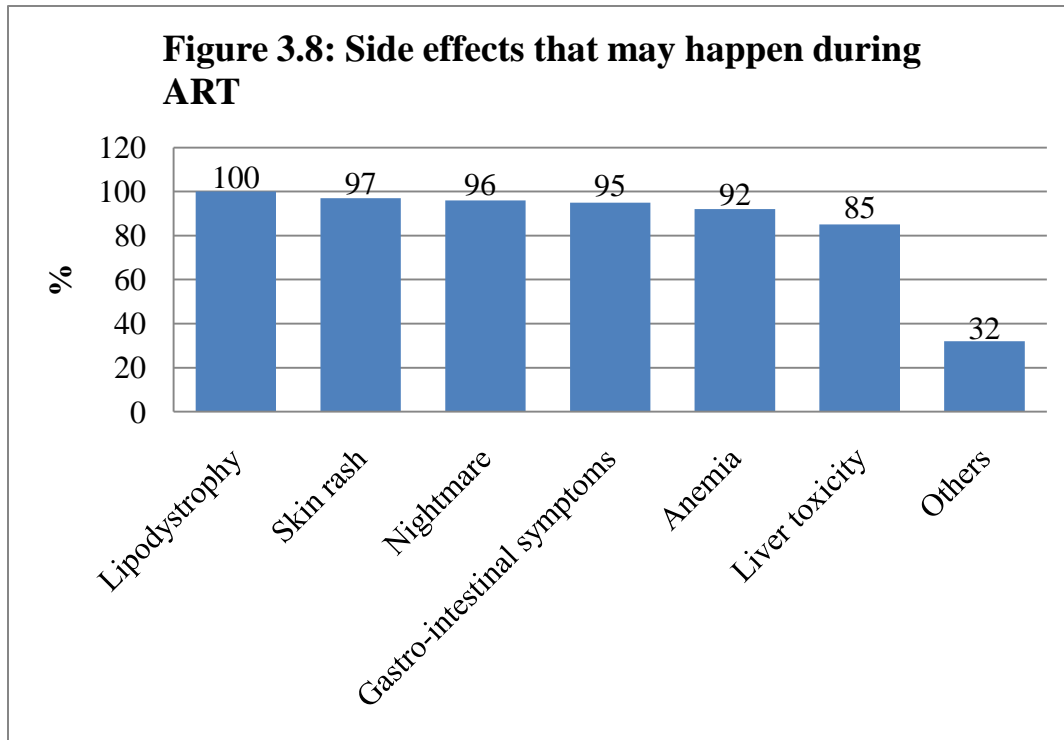
This figure shows that almost 100 percent of respondents were sure that the side effect of ART was lipodystrophy, which is the atrophy of the muscle. Patients remember this side effect because it can affect their beauty such as face and buttock thinning while taking ARVs for at least six months.

3.2.2.5. What will you do if side effects happen?

Table 3.7 demonstrates that going to hospital was the best way when side effects occur. Among several possible answers, 99 percent of the patients said that they would call doctor for advice if side effects occur. Moreover, all patients said they would go to hospital for consulting with doctor. Nobody would stop taking ARVs or buy drugs from pharmacy to treat side effects.

Table 3.7: Measures to be taken when side effects happen

	Stop taking ARV by myself	Buy drug from pharmacy to treat side effects	Call doctor for advice	Go to hospital for consulting with doctor	Do not know	Others
N Valid	0	0	116	117	0	5
Missing	117	117	1	0	117	112

Note: Missing numbers in this table are the numbers of patients who did not respond or choose the answers.

3.2.2.6. What are the benefits of taking ARV regularly, continuously, and correctly?

Table 3.8: Benefits of taking ARVs regularly, continuously, and correctly

	Suppression of HIV viral load in blood	Avoidance of resistance of HIV to ART	Achievement of ART success	Do not know	Others
N Valid	115	115	115	1	30
Missing	2	2	2	116	87

Note: Missing numbers in this table are the numbers of patients who did not respond or choose the answers.

Table 3.8 shows that almost all patients (98 percent) knew the benefits of taking ARVs regularly, continuously, and correctly very well, saying that they take ARV to suppress HIV viral load in blood and to avoid resistance of HIV to ART or to achieve ART success. The remaining 30 out of the 117 patients provided other possible answers. 13 out of the 30 patients said that the benefits of taking ARVs

regularly, continuously, and correctly were good health, followed by nine high CD4, and eight prolonged life, prevention of opportunistic infections, HIV transmission, and reduction of HIV viral load in blood.

After summing up all knowledge scores of the total six questions above, the author is able to calculate and assess the patients' knowledge scores as in the table below.

3.2.2.7. Levels of ART knowledge

Figure 3.9: Levels of ART knowledge of research participants
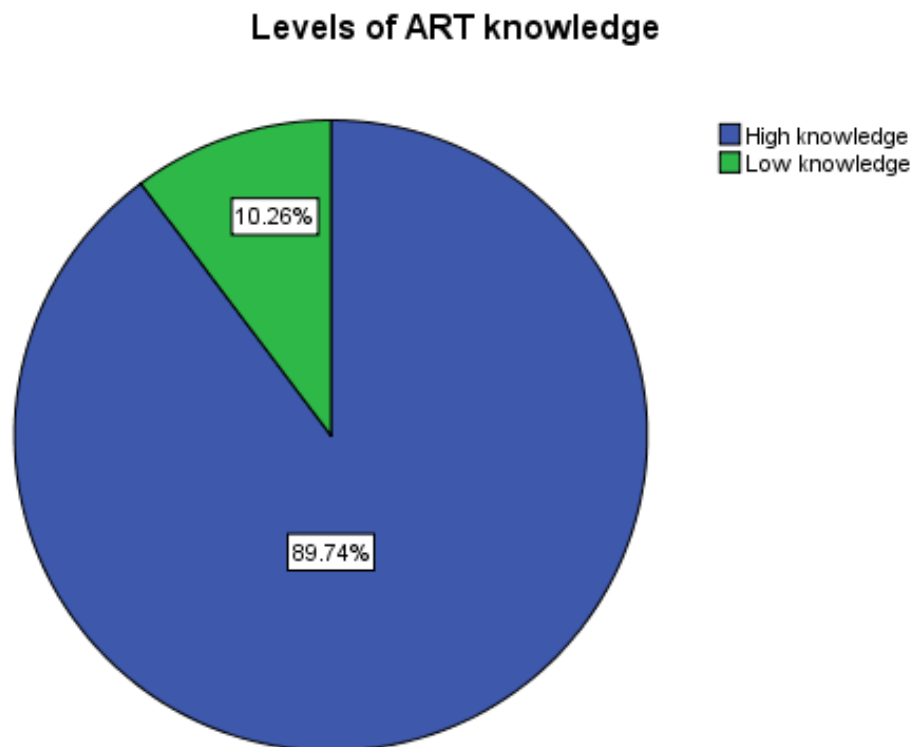
This pie chart reveals that almost all (89.7%) of the total research participants had high knowledge of ART, whereas the remaining 10.3 percent represented low knowledge of ART. Even though patients had a high level of ART knowledge, some of them still showed poor adherence to ART.

3.2.3. Treatment regimens and OI treatments of the research participants

3.2.3.1. ART regimens

The quality of life of the HIV/AIDS patients cannot be improved unless they take Antiretroviral drugs (ARV) appropriately and correctly. At Sihanouk Hospital Center of HOPE (SHCH), there are two kinds of ART regimens (Sihanouk Hospital Center of HOPE, 2008). The first regimen is first-line ART and the second regimen is second-line ART. Patients are provided first with the first-line ART, while the second-line ART is indicated when the HIV is resistant to the first-line ART or in case of first-line ART failure. In addition, second-line ART has higher pill burden than that of first-line ART and its cost is around 10 times higher than that of first-line ART.

What ART drugs are you currently on?

In table 3.9, there are two ART lines. First-line ART contains seven ART regimens such as 3TC+EFV+AZT, 3TC+EFV+TDF, 3TC+NVP+AZT, 3TC+NVP+TDF, ABC+3TC+EFV, D4T+3TC+EFV, and D4T+3TC+NVP, while second-line ART has 4 ART regimens such as 3TC+TDF+KALETRA, 3TC+TDF+KALETRA+AZT, ABC+DDI+KALETRA, and D4T+3TC+KALETRA.

Almost all of the HIV/AIDS patients (90 percent) were on the first-line ART, while the second-line ART accounted for only 10 percent. 3TC+NVP+AZT, D4T+3TC+NVP, and D4T+3TC+EFV regimens accounted for 35, 21, and 14 percent respectively, whereas the remaining ART regimens represented very low percentages.

Table 3.9: ART regimens

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	3TC+EFV+AZT	11	9.4	9.4	9.4
	3TC+EFV+TDF	4	3.4	3.4	12.8
	3TC+NVP+AZT	41	35.0	35.0	47.9
	3TC+NVP+TDF	7	6.0	6.0	53.8
	3TC+TDF+KALETRA	4	3.4	3.4	57.3
	3TC+TDF+KALETRA+AZT	4	3.4	3.4	60.7
	ABC+3TC+EFV	1	.9	.9	61.5
	ABC+DDI+KALETRA	1	.9	.9	62.4
	D4T+3TC+EFV	17	14.5	14.5	76.9
	D4T+3TC+KALETRA	2	1.7	1.7	78.6
	D4T+3TC+NVP	25	21.4	21.4	100.0
	Total	117	100.0	100.0	

3.2.3.2. OI drug treatments

Opportunistic Infection (OI) drugs are medicines other than ART drugs used by the HIV/AIDS patients to treat opportunistic infections such as tuberculosis, pneumonia, diarrhea, skin diseases, sexually transmitted diseases, meningitis, heart diseases, liver diseases, kidney diseases, and other opportunistic diseases that might occur in the patients. Moreover, drugs that are used to prevent the occurring of

opportunistic infections, for example, fungal infections and Pneumocystis Carinii

Pneumonia (PCP), severe disease of lungs, also represent OI drugs.

What other drugs (beside antiretroviral) are you currently on?

3.2.3.2.1. OI drug use

Figure 3.10: OI Drug use of research participants
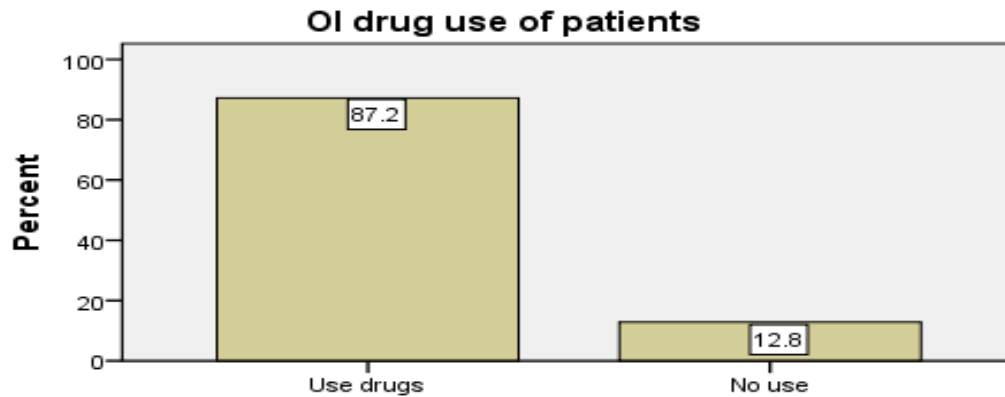
Figure 3.10 illustrates that most all of the patients (87 percent) took

opportunistic infection drugs, while the rest, 13 percent, did not take the medicines.

HIV/AIDS patients used OI drugs because they had opportunistic infections and were

not healthy.

Figure 3.11 shows that pain killers were the medicine that the majority of the

HIV/AIDS patients (67.5 percent) were taking to relieve their pains; appetite

stimulants/vitamins were also popular among the patients with 52 percent of the

patients taking them. Antibiotics, TB drugs, sleeping pills, and fluconazole

prophylaxis were taken by a small number of the patients, with less than 10 percent of

the patients taking them. Patients took the two most popular OI drugs, pain killers and

vitamins, because they had severe OIs and weak physical conditions. Therefore, they

needed to take these drugs in order to reduce their pains and strengthen their power.

Figure 3.11: OI drugs taken
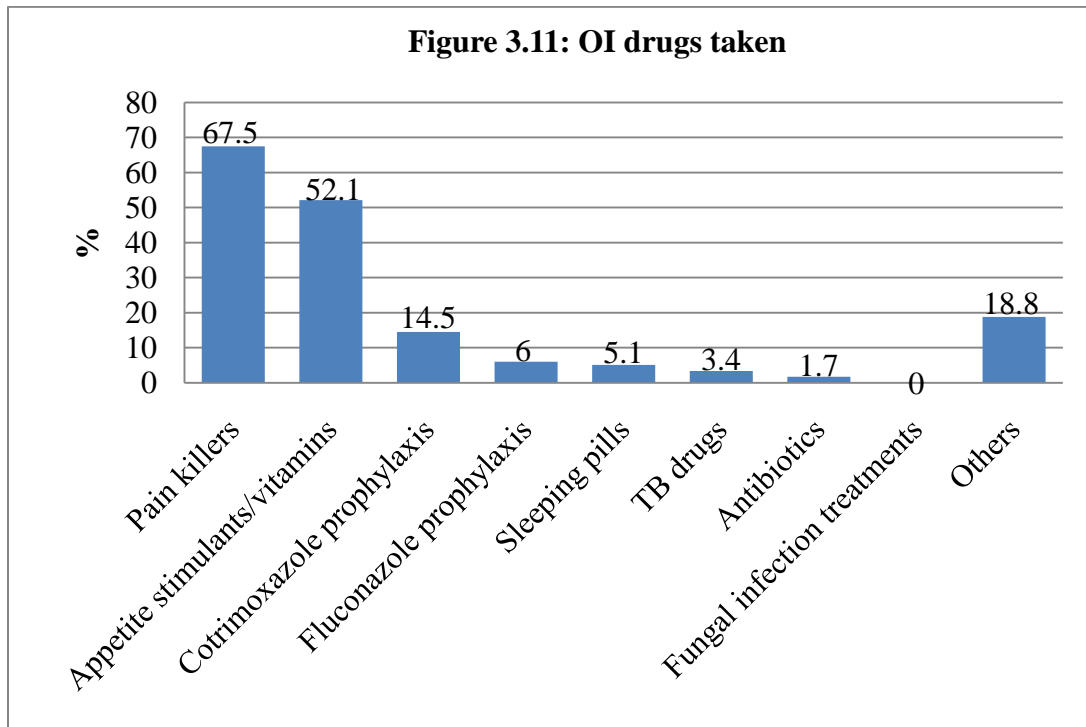
3.2.3.2.2. Number of times taking OI drugs

Taking OI drugs more frequently might cause patients to take their ARVs irregularly or incorrectly.

Number of times taking OI drugs was calculated according to the names of the drugs. For instance, one tablet of OI drug was considered as one time taking OI drug, two different OI drugs considered as two times, and three OI drugs as three times.

Figure 3.12: Number of time taking OI drugs
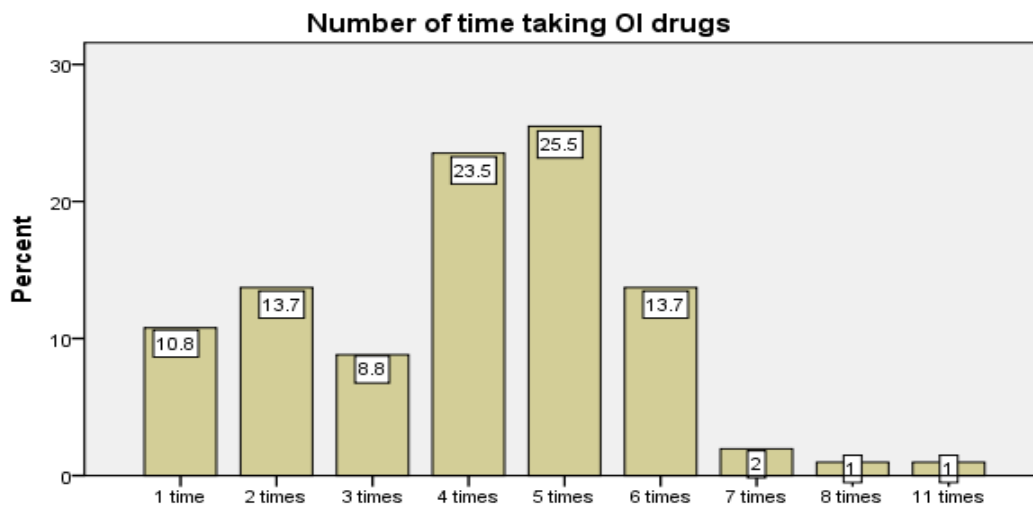
The graph shows that 4 and 5 times taking OI drugs accounted for the majority, 25 and 23 percent, respectively, while 2 times and 6 times taking OI drugs represented the same percent, 14. Whereas 1 time and 3 times taking OI drugs accounted for 11 and 9 percent, respectively. The remaining times taking OI drugs, however, showed the smallest percents.

3.2.3.2.3. Number of types of OI drugs

The more OI drugs the patients take, the more pill burdens they have. High pill burdens of OI medicines are more likely to cause patients not to adhere to ART adherence. Different names of OI drugs have different types.

The figure 3.13 shows that HIV/AIDS patients taking 1 type and 2 types of OI drugs represented 32 and 35 percent, respectively, while taking 3 types accounted for 14 percent. Not taking any OI drugs consisted of 13 percent, whereas the rest showed the smallest percents.

Figure 3.13: Number of OI drug types

Number of OI types

Legend:
- Not taking OI drugs
- Taking 1 type
- Taking 2 types
- Taking 3 types
- Taking 4 types
- Taking 5 types
- Taking 6 types

12.82%
0.85%
14.53%
32.48%
35.04%
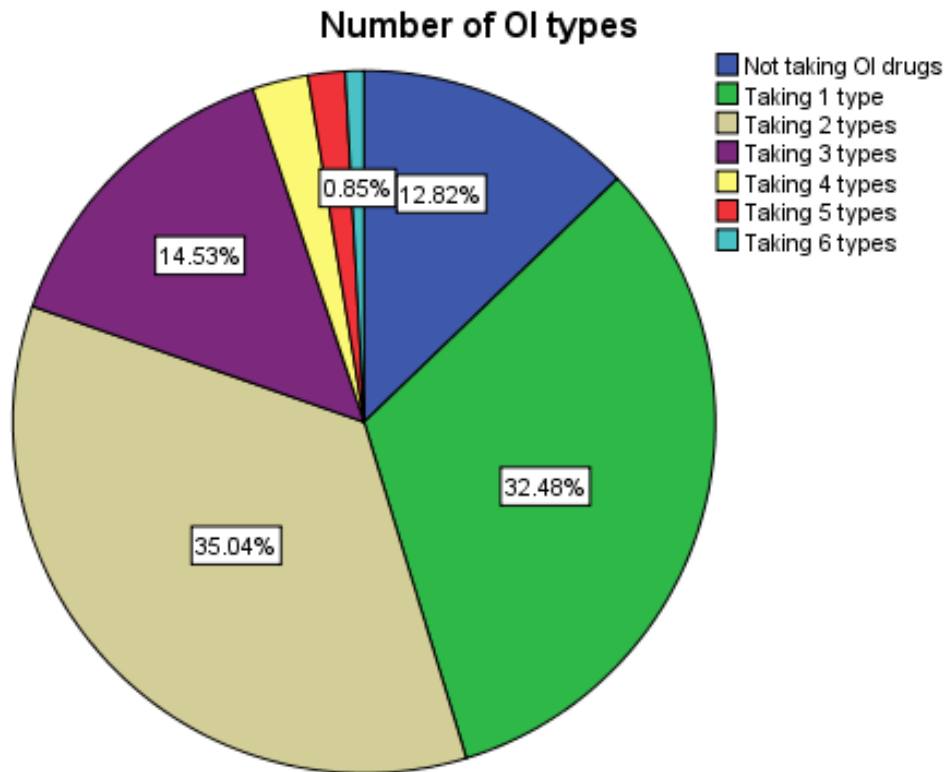
3.2.3.3. Difficulty taking ARVs while taking OI drugs

Table 3.10: Difficulty taking ARVs

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Not taking OI drugs	15	12.8	12.8	12.8
	Difficulty	5	4.3	4.3	17.1
	No difficulty	97	82.9	82.9	100.0
	Total	117	100.0	100.0	

This table illustrates that among the total 117 research respondents, 13 percent did not take OI drugs. Most of the patients, 102 (87 percent) took OI drugs; however,

83 percent of them had no difficulty taking ARVs while using OI drugs. This indicates that taking OI drugs did not cause any problems of taking ART at all. The main reasons for not having difficulty taking tablets were that patients took ARVs and OI drugs separately, at different times; also, they had high commitment of taking their medicines, through reminding of their family members, relatives as well as their neighbors; some ART drugs are combined into one tablet, and taking drugs is as their habits. Nevertheless, only a minority of the participants had difficulty taking their ARVs due to some reasons, namely too many pill burdens, many times of taking their medicines, and ART side effects, especially nausea and vomiting.

3.2.4. Side effects of ART of research participants

In the side effects section, the author asked three questions from participants in order to get information on side effects of ART and its related characteristics.

While taking ARVs, HIV/AIDS patients may encounter intolerant or adverse effects of the ART. There are, in fact, two kinds of ART side effects, short-term and long-term after taking ARVs. Short–term side effects can occur within six months of taking ARVs, including headache, nausea, vomiting, abdominal pain, nightmare, skin rash, diarrhea, liver toxicity, and others. While long-term side effects may happen while taking ARVs for at least six months; the long-term side effects are numbness of limbs, lipodystrophy, pancreatitis, anemia, and change in nail color. Side effects might influence adherence to ART.

3.2.4.1. Did you experience drug side effects?

Figure 3.14: Patients' experience of ART side effects
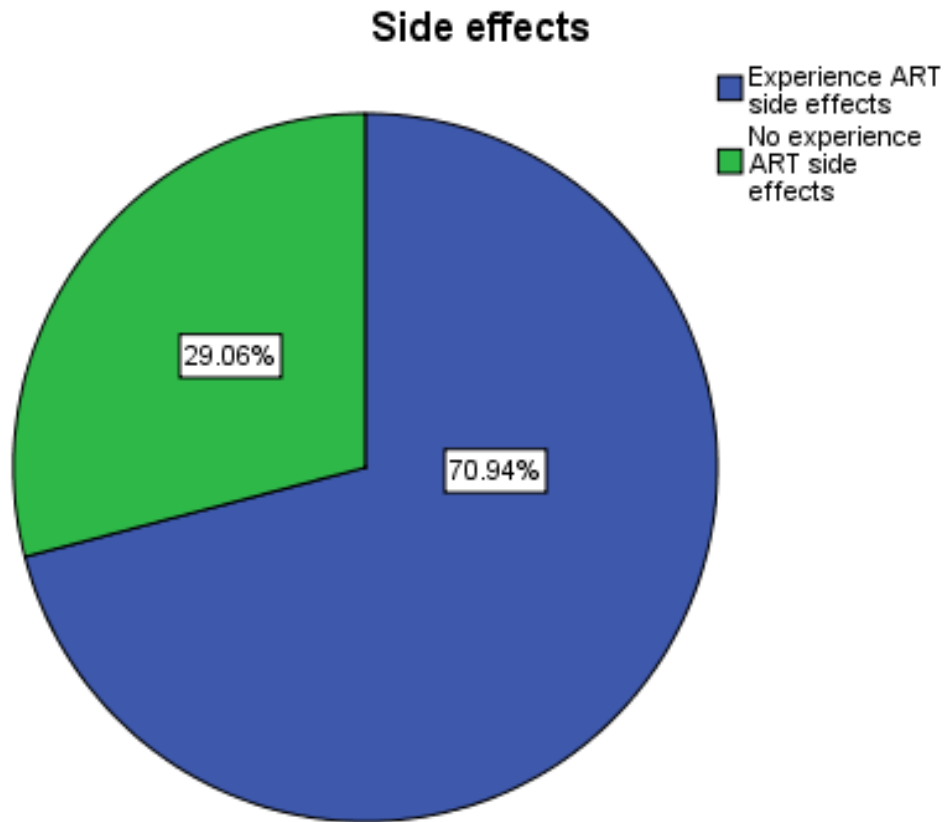
This pie chart shows that the majority of all 117 research respondents (71 percent) experienced side effects, while 29 percent did not experience side effects of ART. After taking ARVs, some HIV/AIDS patients might encounter side effects, of which some are minor; however, some are more serious and even deadly.

Figure 3.15: ART side effects that patients experienced
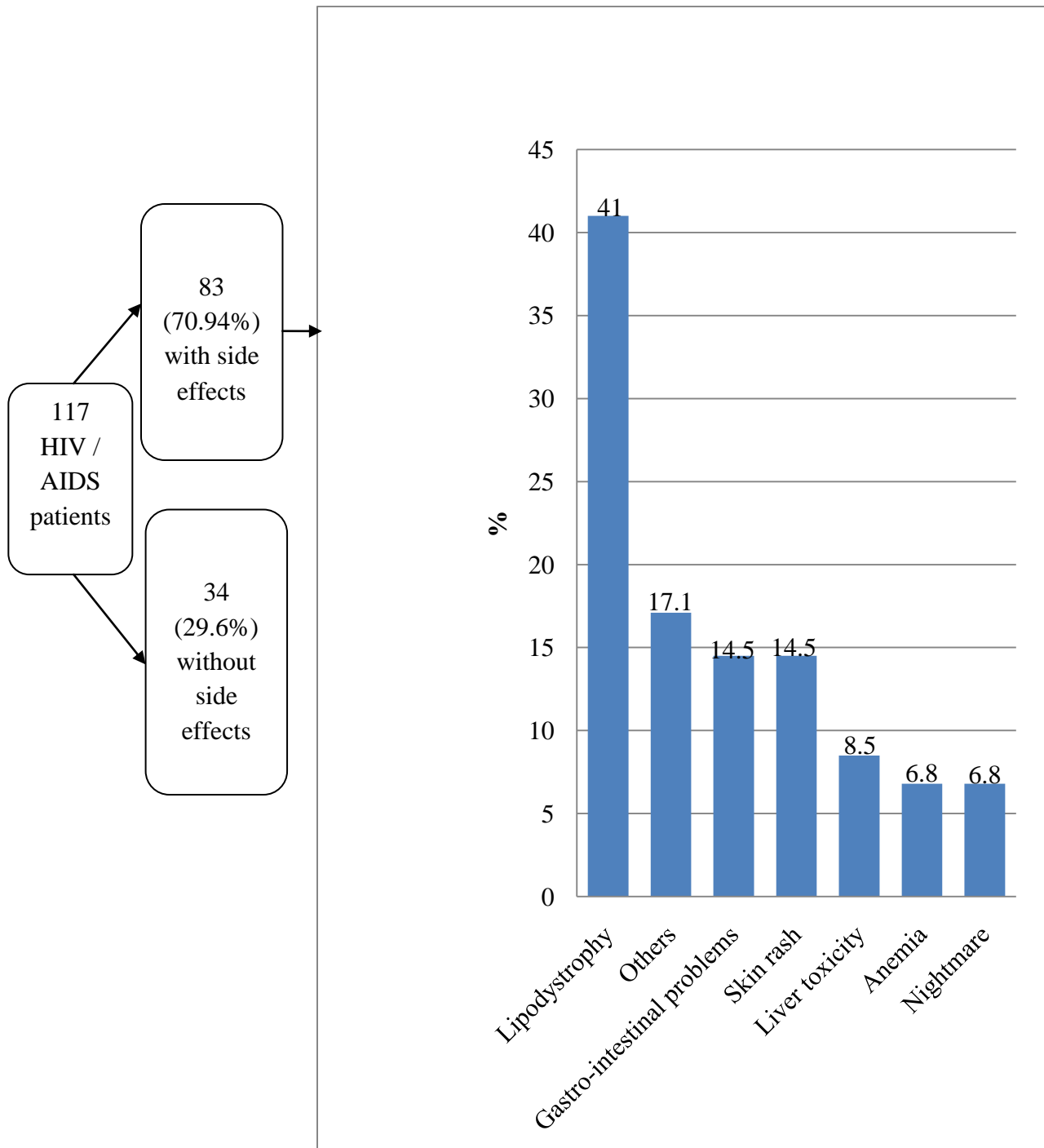
This graph reveals that among the 83 patients who experienced side effect, lipodystrophy was the leading side effect (41 percent), followed by gastro-intestinal and skin rash side effects, with the same percent, 14. Other side effects, 17 percent, were leg numbness, toxicity of nervous system, high fever, blurred vision, and even blindness. The rest, however, was the minority.

3.2.4.3. Did side effects cause you to stop taking the medicine?

Figure 3.16: Stop and no stop taking ART
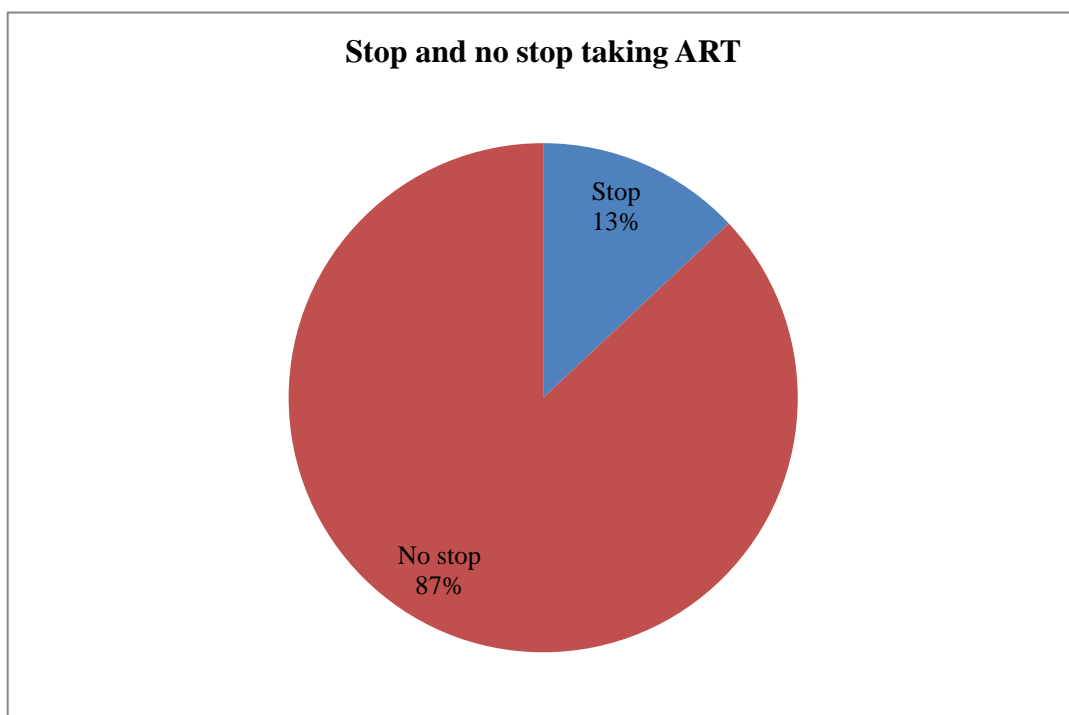
This pie chart illustrates that side effects were subjectively not a major barrier to taking ART drugs. Of those 82 patients who said they experienced side effects, only about 13 percent said side effects caused them to stop taking the medicines,

while 87 percent said the side effects did not stop them from taking the medicine. Even though the research respondents mentioned that side effects did not cause them to stop taking their ARVs, it is not sure whether it is the case or not. Therefore, a statistical analysis is needed in order to prove it.

3.2.5. Reasons reported for missing ART doses in this study

3.2.5.1. Did you take ARVs regularly and correctly?
Table 3.11: Taking ARVs regularly, continuously, and correctly

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Yes	55	47.0	47.0	47.0
	No	62	53.0	53.0	100.0
	Total	117	100.0	100.0	

The majority of the surveyed patients (53%) did not take ARVs regularly and correctly while 47 % said they did.

3.2.5.2. What are the factors that help you take ARVs regularly and correctly?
Most of the patients said alarm clock helped them take ARVs regularly and correctly.

3.2.5.3. What cause you not to take your tablets?
This question was asked to patients who had poor adherence to ART to seek for reasons that caused patients not to take their medicines generally.

Figure 3.17: Causes not to take ARVs
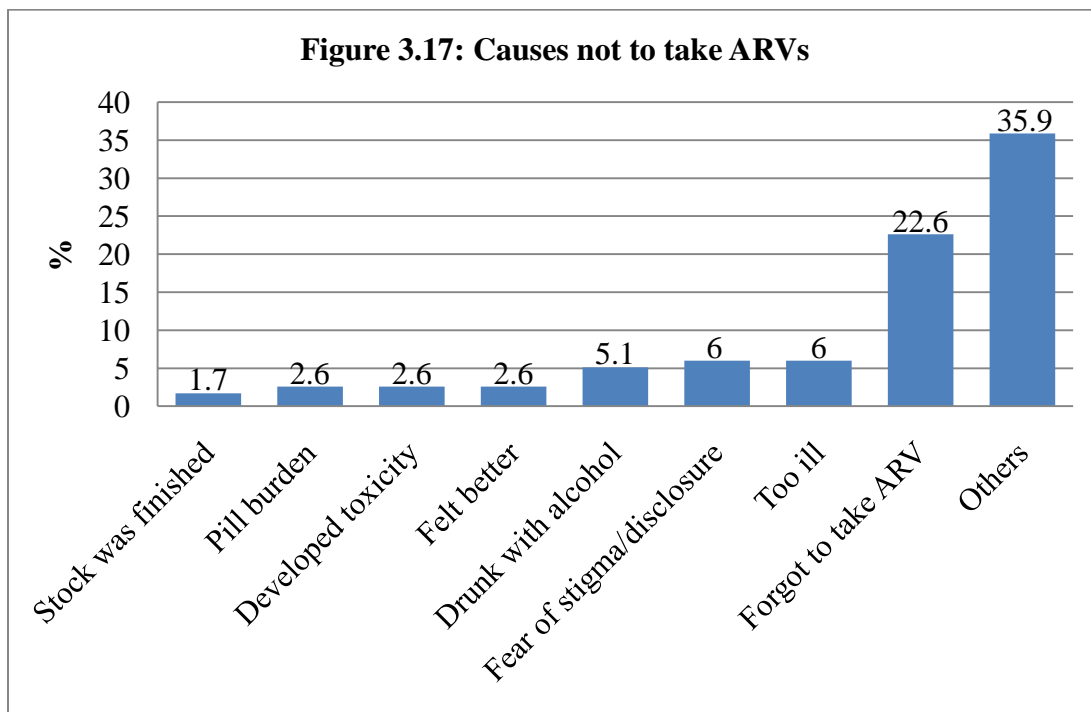
This figure shows that one of the major causes of not taking tablets was forgetting (22.2%) to take ART tablets. Only six percent of the patients said that feeling very ill was the cause of not taking their tablets. The same percentage said fear of stigma/disclosure was also the cause. It is understood that most of the patients had enough stock of tablets to take. Only 1.7 percent said finished stock was the cause of not taking their tablets. The remaining 35.9 percent of reasons for not taking their ARVs were mostly due to being busy with their works, followed by conflicts with their family members as well as neighbors, taking care of their children, lack of time reminders such as cell phones and alarm clocks.

3.2.5.4. Many people find it hard to remember to take every single dose; in the last one month, how many doses have you missed?

This question was asked to the patients to investigate whether the patients missed their ART doses one month prior to the interviews or not. By doing this, adherence to ART was found. In addition, one tablet of each ART drug means one dose; having failed to take one tablet means missing one dose of ART. Furthermore, missing ART more than three doses per month represents poor adherence to ART.

Figure 3.18: Status of ARV doses in the last month prior to interviews
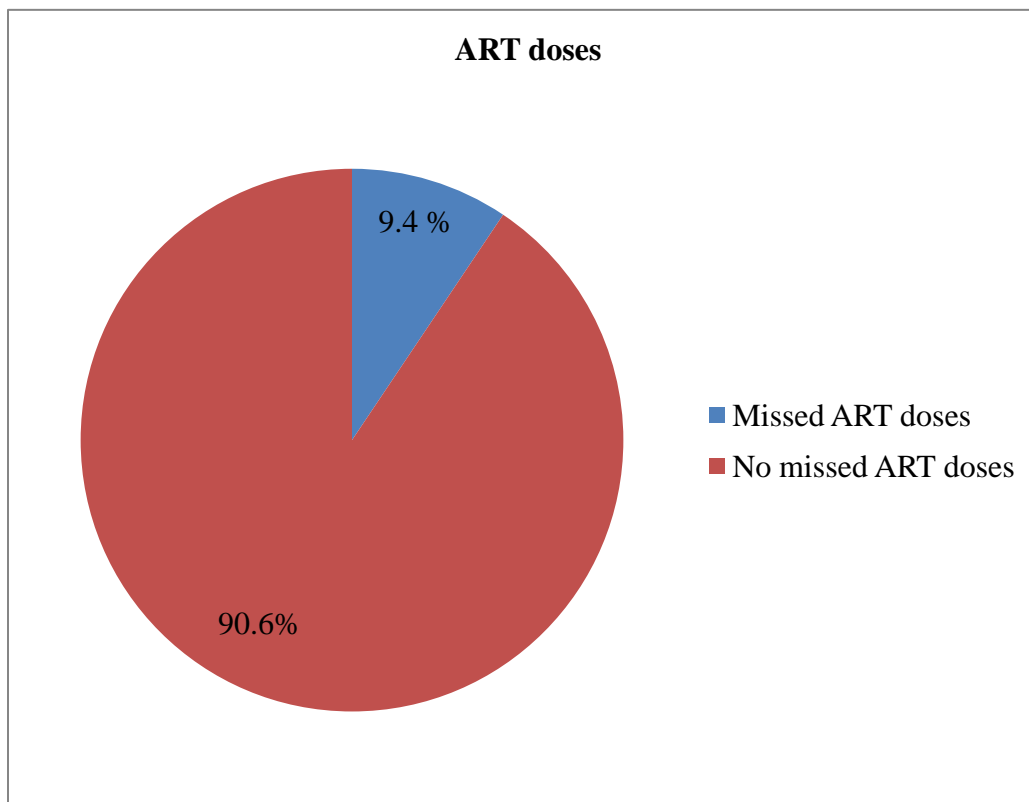
This pie chart shows that the majority of the research respondents, 106 (90.6%) out of the 117 patients did not miss their ART doses. Nevertheless, only 11 (9.4%) of the patients missed their ART doses. Note that the patients subjectively provided the answers.

3.2.5.5. ARV drugs and its doses missed one month prior to interviews
Table 3.12: ARV drugs and its doses missed one month prior to interviews

Patient	D4T	3TC	EFV	NVP	TDF	KALETRA	AZT
1	1	1					
2	1	1		1			
3	1	1		1			
4		2	1		1		
5	2	2		2			
6	4	4					
7	6	6	3				
8	5	5				10	
9		20	10				20
10	28	28	14				
11	120	120		120			

This table demonstrates that 11 (9.4%) out of 117 patients missed their ART doses one month prior to the interview. Each patient missed at least two doses of ART, for example, patient number 1 missed two doses, which was calculated by adding one dose of D4T to another dose of 3TC. Remarkably, patient number 9, 10, and number 11 each had missed 50 doses, 70 doses, and 360 doses of ART, respectively. Family conflicts; natural disasters, such as floods, which cut off the roads; and lack of money for transportation fees, were the causes of failing to take their ART doses. Patient number 11 had exclusively missed her ART doses because

of prolonging her stay to another two months in the United States. Eight (about 73%) out of 11 patients missed their ARVs more than three doses one month before the interview. This means that about 73% of 11 respondents who missed their medication doses were poor ART adherent patients (missed more than three doses in the last month prior to the interview) or eight (about 7%) of 117 were poor ART adherent patients. Therefore, poor ART adherence still exists.

3.3. Results of association between dependent and independent variable analysis

This section is divided into two parts. The first part is hypothesis testing such as drug side effects versus adherence to ART, ART regimens versus adherence to ART, OI drug uses versus adherence to ART, knowledge of HIV/AIDS patients on ART versus adherence to ART, educational levels versus adherence to ART, patient's location of residence versus adherence to ART, and poverty versus adherence to ART. The second part is other socio-demographic and economic factors and adherence to ART testing such as WHO stages versus adherence to ART, CD4 groups versus adherence to ART, sex versus adherence to ART, age groups versus adherence to ART, marital status versus adherence to ART, occupation versus adherence to ART, and food versus adherence to ART.

3.3.1. Hypothesis testing

3.3.1.1. Results of association between side effects of ART and adherence to ART analysis

      Based on two kinds of adherence status of the respondents, poor and good adherent patients to ART, this section was divided into two parts: side effects versus adherence status cross-tabulation, and the statistical test, Chi-square to show whether there is any statistically significant association between side effects and adherence status or not. Cross-tabulations were performed only with hypothesis testing.

3.3.1.1.1. ART side effects versus adherence status cross tabulation

Table 3.13: Side effects versus adherence status cross-tabulation

			Adherence status		
			Poor	Good	Total
Side effects	Experience ART side effects	Count	36	47	83
		% within Side effects	43.4%	56.6%	100.0%
		% within Adherence status	60.0%	82.5%	70.9%
		% of Total	30.8%	40.2%	70.9%
	No experience ART side effects	Count	24	10	34
		% within Side effects	70.6%	29.4%	100.0%
		% within Adherence status	40.0%	17.5%	29.1%
		% of Total	20.5%	8.5%	29.1%
	Total	Count	60	57	117
		% within Side effects	51.3%	48.7%	100.0%
		% within Adherence status	100.0%	100.0%	100.0%
		% of Total	51.3%	48.7%	100.0%

This table shows that the data classify 117 research respondents by side effects (experience side effects /no experience side effects) and adherence status (poor/good). The author ran the cross-tabulation procedure with side effects as the row variable and adherence status as the column variable.

The top number in each cell is *the count*. The cell counts indicate that 36 poor adherent and 47 good adherent patients experienced side effects of ART; 24 poor adherent and 10 good adherent patients did not experience side effects of ART. Furthermore, the marginal counts indicate that 83 and 34 patients experienced and did not experience side effects, respectively and that there were 60 and 57 poor and good adherent patients, respectively. The total number of cases in the table is 117, which appears on the bottom-right hand corner of the table.

The marginal percentages represent *the percentage of the total* that is found in the row or column. For instance, of the entire sample of 117 patients, 83 of them (70.9%) experienced side effects, while 34 (29.1%) of them did not experience side effects. Moreover, 51.3% of all of the patients were poor adherent patients, while 48.7% were good adherent patients.

Below the count is *the % within side effects or the row percentage*, which represents the percentage of the row that is found in the cell. For example, 43.4% of all patients who experienced side effects were poor adherent patients, while 56.6% were good adherent patients.

While the third number, *% within adherence status*, in each cell is the column percentage or percentage of poor or good adherent patients, who experienced or did not experience side effects. Taken as an example, 60.0% of the 60 poor adherent patients experienced side effects, however, 40.0% did not experience side effects. In addition, 82.5% of the 57good adherent patients experienced side effects, while 17.5% of them did not experience side effects.

The last line of each cell, labeled *% of total*, indicates the total percentage. 36 poor adherent patients, who experienced drug side effects, represented 30.8% of all 117 patients, while 24 (20.5%) were poor adherent patients who did not have experience of drug side effects. In addition, 40.2% of the total sample were good adherent patients who experienced side effects, while 8.5% were good adherent patients who did not experience side effects.

Although there were different percentages between poor adherent patients (43.4%) and good adherent patients (56.6%) of the total 83 patients who experienced side effects, in this small sample there is probably a weak strength of association between drug side effects and adherence to ART. Therefore, a statistical significance test such as Chi-square is needed to measure the strength of association between dependent variable (adherence status) and independent variable (side effects).

3.3.1.1.2. Chi-square test for association between ART side effects and adherence to ART

Table 3.14: Chi-square test for association between ART side effects and adherence to ART

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	7.150[a]	1	.007		
Continuity Correction	6.102	1	.013		
Likelihood Ratio	7.325	1	.007		
Fisher's Exact Test				.009	.006
Linear-by-Linear Association	7.089	1	.008		
N of Valid Cases	117				

a. 0 cells (.0%) have expected count less than 5. The minimum expected count is 16.56.
b. Computed only for a 2x2 table

3.3.1.1.3. Chi-square test for association between gastro-intestinal side effects and adherence to ART Analysis

Table 3.15: Chi-square test for association between gastro-intestinal side effects and adherence to ART

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	9.535[a]	1	.002		
Continuity Correction	7.916	1	.005		
Likelihood Ratio	9.712	1	.002		
Fisher's Exact Test				.003	.002
Linear-by-Linear Association	9.420	1	.002		
N of Valid Cases	83				

a. 0 cells (.0%) have expected count less than 5. The minimum expected count is 7.37.
b. Computed only for a 2x2 table

Table 3.14 shows that there was a statistically significant association between drug side effects and adherence to ART (X²=7.150, df =1, P-value (Asymp Sig.)=0.007).

Table 3.15 demonstrates that, of all the side effects that patients experienced, only gastro-intestinal side effects such as nausea, vomiting, and abdominal pain are statistically significantly associated with adherence to ART (X²= 9.535, df= 1, P-value= 0.002).

3.3.1.2. Results of association between treatment ART regimens and adherence to ART of the research participants

3.3.1.2.1. ART regimens versus adherence status cross-tabulation

At Sihanouk Hospital Center of HOPE (SHCH) and in Cambodia, there are only two ART line regimens, first-line and second-line ART regimens. First-line ART regimen consists of seven regimens such as 3TC+EFV+AZT , 3TC+EFV+TDF, 3TC+NVP+AZT, 3TC+NVP+TDF, ABC+3TC+EFV, D4T+3TC+EFV, and D4T+3TC+NVP, while second-line ART regimen is composed of four regimens such as 3TC+TDF+KALETRA, 3TC+TDF+KALETRA+AZT, ABC+DDI+KALETRA, and D4T+3TC+KALETRA.

Table 3.16: ART regimens versus adherence status cross-tabulation

			Adherence status		Total
			Poor	Good	
ART regimens	First-line ART regimens	Count	55	51	106
		% within ART regimens	51.9%	48.1%	100.0%
		% within Adherence status	91.7%	89.5%	90.6%
		% of Total	47.0%	43.6%	90.6%
	Second-line ART regimens	Count	5	6	11
		% within ART regimens	45.5%	54.5%	100.0%
		% within Adherence status	8.3%	10.5%	9.4%
		% of Total	4.3%	5.1%	9.4%
	Total	Count	60	57	117
		% within ART regimens	51.3%	48.7%	100.0%
		% within Adherence status	100.0%	100.0%	100.0%
		% of Total	51.3%	48.7%	100.0%

This table illustrates that almost all patients, 106 (90.6%) of the total 117 patients, were on first-line ART regimens, while 11 (9.4%) patients were on second-line ART regimens. Among 106 patients who were on first-line ART, 55 and 51 patients belonged to poor adherent and good adherent patient groups, respectively. Among 11 patients who were on second-line ART, five and six patients belonged to poor adherent and good adherent patients, respectively. Furthermore, there is not a big difference between poor adherent and good adherent patients who use first-line ART regimens. Similarly, there is also not a big difference between poor adherent and good adherent patients who were on second-line ART regimens. Based on this context, statistical test, Chi-square is needed in order to make sure whether there is

any statistically significant association between ART drug regimens and adherence to ART or not.

3.3.1.2.2. Chi-square test for association between ART regimens and adherence to ART

After running a Chi-square test in the SPSS version 18, the result shows that there was no statistically significant association between ART regimens and adherence to ART (X^2= 0.165, df= 1, P-value= 0.685).

3.3.1.3. Results of association between OI Drug uses and adherence to ART analysis

3.3.1.3.1. OI drug uses versus adherence status cross-tabulation

The table 3.17 shows that the majority of the patients, 102 (87.2%) of the entire 117 sample, used OI drugs, while only 15 (12.8%) did not use them. As can be seen in the table, the number of poor adherent patients (52) and good adherent patients (50) who used OI drugs is similar. Also, there is almost the same number of poor adherent and good adherent patients who did not use OI drugs. In addition, it is not sure whether any association between OI drug uses and adherence to ART exists or not. Therefore, a statistical test is needed for evidence.

Table 3.17: OI drug use of patients versus adherence status cross-tabulation

			Adherence status		Total
			Poor	Good	
OI drug use of patients	Use drugs	Count	52	50	102
		% within OI drug use of patients	51.0%	49.0%	100.0%
		% within Adherence status	86.7%	87.7%	87.2%
		% of Total	44.4%	42.7%	87.2%
	No use	Count	8	7	15
		% within OI drug use of patients	53.3%	46.7%	100.0%
		% within Adherence status	13.3%	12.3%	12.8%
		% of Total	6.8%	6.0%	12.8%
Total		Count	60	57	117
		% within OI drug use of patients	51.3%	48.7%	100.0%
		% within Adherence status	100.0%	100.0%	100.0%
		% of Total	51.3%	48.7%	100.0%

3.3.1.3.2. Chi-square test for association between OI drug uses and adherence to ART analysis

The Chi-square test result shows that there is no statistically significant association between OI drug uses and adherence to ART because of (X^2= 0.29, df= 1, P value= 0.865).

3.3.1.4. Results of association between knowledge levels of HIV/AIDS patients of ART and adherence to ART analysis

3.3.1.4.1. ART knowledge levels versus adherence status cross-tabulation

ART knowledge levels were divided into two groups, high knowledge level and low knowledge level. High ART knowledge level was defined with the answer score higher than or equal to 15, while low ART knowledge level with the answer score lower than or equal to 14, and the maximum accurate answer score was 16.

Table 3.18: ART knowledge levels versus adherence status cross-tabulation

| | | | Adherence status | | Total |
			Poor	Good	
ART knowledge	High knowledge	Count	54	51	105
		% within ART knowledge	51.4%	48.6%	100.0%
		% within Adherence status	90.0%	89.5%	89.7%
		% of Total	46.2%	43.6%	89.7%
	Low knowledge	Count	6	6	12
		% within ART knowledge	50.0%	50.0%	100.0%
		% within Adherence status	10.0%	10.5%	10.3%
		% of Total	5.1%	5.1%	10.3%
Total		Count	60	57	117
		% within ART knowledge	51.3%	48.7%	100.0%
		% within Adherence status	100.0%	100.0%	100.0%
		% of Total	51.3%	48.7%	100.0%

This table demonstrates that the majority, 105 (89.7%) of the total 117 respondents had a high knowledge level, while only 12 (10.3%) had a low knowledge level of ART. However, there was no big difference between poor and good adherent patients, who had a high knowledge level. Furthermore, the number of poor and good

adherent patients who had a low knowledge level of ART was the same. Therefore, it is unlikely that there is an association between knowledge of ART and adherence to ART. To identify if there is any association between ART knowledge and adherence or not, Chi-square test is necessary.

3.3.1.4.2. Chi-square test for association between ART knowledge level and adherence to ART

There is no statistically significant association found between ART knowledge and adherence to ART (X^2= 0.009, df=1, P-value= 0.925).

3.3.1.5. Results of association between educational levels and adherence to ART analysis

3.3.1.5.1. Educational levels versus adherence status cross-tabulation

Table 3.19 illustrates that there are four levels of education such as illiterate, primary school, secondary school, as well as high school and university. 31 (26.5%), 40 (34.2%), 27 (23.1%), and 19 (16.2%) of all the entire sample 117 patients represented illiterate, primary school, secondary school, and high school or university, respectively. Moreover, illiterate respondents mean that they cannot read, write, and understand Khmer language as their mother tongue. 26.5% illiterate among the 117 study participants are remarkably high. The number of patients, who had attended primary school, is the largest of all educational levels, 34.2%. As can be seen in the table, except for primary school, the higher the levels of education, the lower the numbers they are. There 19 poor adherent patients out of 31 who are illiterate, while good adherent patients accounted for only 12. Similarly, the numbers

of poor and good adherent patients in primary school and secondary school levels of education are not so different. Noticeably, among the 19 research participants who had attended high school or university, there were seven poor adherent patients, while good adherent patients accounted for 12, which is nearly double the number of poor adherent patients. Although there is not a big difference between the numbers of poor and good adherent patients in each level of education, except for high school or university level, it is necessary to have a significance test to measure if any association between educational levels and adherence to ART exists or not.

Table 3.19: Education revels versus adherence status cross-tabulation

			Adherence status		
			Poor	Good	Total
Educational levels	Illiterate	Count	19	12	31
		% within Educational levels	61.3%	38.7%	100.0%
		% within Adherence status	31.7%	21.1%	26.5%
		% of Total	16.2%	10.3%	26.5%
	Primary school	Count	22	18	40
		% within Educational levels	55.0%	45.0%	100.0%
		% within Adherence status	36.7%	31.6%	34.2%
		% of Total	18.8%	15.4%	34.2%
	Secondary school	Count	12	15	27
		% within Educational levels	44.4%	55.6%	100.0%
		% within Adherence status	20.0%	26.3%	23.1%
		% of Total	10.3%	12.8%	23.1%
	High school or university	Count	7	12	19
		% within Educational levels	36.8%	63.2%	100.0%
		% within Adherence status	11.7%	21.1%	16.2%
		% of Total	6.0%	10.3%	16.2%
Total		Count	60	57	117
		% within Educational levels	51.3%	48.7%	100.0%
		% within Adherence status	100.0%	100.0%	100.0%
		% of Total	51.3%	48.7%	100.0%

3.3.1.5.2. Chi-square test for association between educational levels and adherence to ART

There is no statistically significant association between education of research participants and ART adherence because (X^2= 3.555, df= 3, P-value= 0.314).

3.3.1.6. Results of association between patient's location of residence and adherence to ART analysis

Patient's location of residence was divided into two categories, Phnom Penh and provinces. Phnom Penh is the capital city of Cambodia, which is defined as within about 30 km from the research study, Sihanouk Hospital Center of HOPE, while provinces are at least farther than 30 km away from the research study.

3.3.1.6.1. Patient's location of residence versus adherence status cross-tabulation

Table 3.20 indicates that most of the 117 study participants, 73 (62.4%) lived in Phnom Penh, while 44 (37.6%) lived in provinces. However, the numbers of poor and good adherent patients, who lived in Phnom Penh, were almost the same. Of the 44 patients who lived in provinces, the numbers of poor and good adherent patients were nearly the same, too. Since there was almost no difference between the numbers of poor and good adherent patients living in Phnom Penh and provinces, it is unlikely that an association between patient's location of residence and adherence to ART exists. In order to respond to this context, Chi-square test is in need for confirming the association.

Table 3.20: Patient's location of residence versus adherence status Cross-

tabulation

			Adherence status		Total
			Poor	Good	
Patient's location of residence	Phnom Penh	Count	37	36	73
		% within Patient's location of residence	50.7%	49.3%	100.0%
		% within Adherence status	61.7%	63.2%	62.4%
		% of Total	31.6%	30.8%	62.4%
	Provinces	Count	23	21	44
		% within Patient's location of residence	52.3%	47.7%	100.0%
		% within Adherence status	38.3%	36.8%	37.6%
		% of Total	19.7%	17.9%	37.6%
Total		Count	60	57	117
		% within Patient's location of residence	51.3%	48.7%	100.0%
		% within Adherence status	100.0%	100.0%	100.0%
		% of Total	51.3%	48.7%	100.0%

3.3.1.6.2. Chi-square test for association between patient's location of residence and adherence to ART.

There is no statistically significant association between patient's location of residence and adherence to ART (X^2=0.28, df=1, P-value= 0.868).

3.3.1.7. Results of association between poverty and adherence to ART analysis

3.3.1.7.1. Economic status versus adherence status cross-tabulation

The economic status of the study respondents was classified into two levels, poor and not poor. Poor patients were defined with earning a money income less than or equal to 1US$ (1US$=4000 Riel, local currency) per day, while not poor patients with earning a money income more than 1US$ per day.

Table 3.21 shows that the majority of the total 117 participants, 82 (70.1%) were poor, while 35 (29.9%) were not poor patients. It is clear that among all 82 poor patients, the numbers of poor and good adherent patients were nearly the same, with 42 and 40, respectively. Likewise, there were almost the same number of poor and good adherent patients who were not economically poor, 18 and 17, respectively. For that reason, a statistical test such us Chi-square is needed to confirm whether or not there is any association between poverty and adherence to ART.

Table 3.21: Economic status versus adherence status cross-tabulation

			Adherence status		Total
			Poor	Good	
Economic status	Poor	Count	42	40	82
		% within Economic status	51.2%	48.8%	100.0%
		% within Adherence status	70.0%	70.2%	70.1%
		% of Total	35.9%	34.2%	70.1%
	Not poor	Count	18	17	35
		% within Economic status	51.4%	48.6%	100.0%
		% within Adherence status	30.0%	29.8%	29.9%
		% of Total	15.4%	14.5%	29.9%
	Total	Count	60	57	117
		% within Economic status	51.3%	48.7%	100.0%
		% within Adherence status	100.0%	100.0%	100.0%
		% of Total	51.3%	48.7%	100.0%

3.3.1.7.2. Chi-square test for association between poverty and adherence to ART

There is no any statistically significant association between poverty and adherence to ART (X^2=0.000, df=1, P value=0.983).

3.3.2. Results of association between gender, age groups, CD4 groups, WHO stages, marital status, occupations, food access status and adherence to ART Analysis

3.3.2.1. Results of association between gender and adherence to ART analysis

Table 3.22: Gender versus adherence status cross-tabulation

| | | | Adherence status | | |
			Poor	Good	Total
Gender	Male	Count	26	19	45
		% within Gender	57.8%	42.2%	100.0%
		% within Adherence status	43.3%	33.3%	38.5%
		% of Total	22.2%	16.2%	38.5%
	Female	Count	34	38	72
		% within Gender	47.2%	52.8%	100.0%
		% within Adherence status	56.7%	66.7%	61.5%
		% of Total	29.1%	32.5%	61.5%
Total		Count	60	57	117
		% within Gender	51.3%	48.7%	100.0%
		% within Adherence status	100.0%	100.0%	100.0%
		% of Total	51.3%	48.7%	100.0%

This table indicates that the majority of the research respondents, 72 (61.5%) were females. However, the number of poor and good adherent patients of the total females was not so different, while the number of males accounted for 45 (38.5%) of the entire 117 sample. Also, among the 45 males, the number of poor and good adherent patients was 26 and 19, respectively. There was no statistically significant association between gender and adherence to ART (X^2= 1.235, df= 1, P-value=0.266).

3.3.2.2. Results of association between age groups and adherence to ART analysis

Table 3.23 shows that the number of poor and good adherent patients in the age groups 30-34 and 35-39 years old was almost the same. These two age groups had a greater number than that of the other age groups. Similarly, the number of the age groups 40-44 and older than 44 years old was nearly the same. However, the number of poor and good adherent patients in the age group 30-34 years old was nine and 14, respectively. Of the age group older than 44 years old, poor adherent patients accounted for 14, while good adherent patients were 10, which was slightly different. However, there is no statistically significant association between age groups and adherence to ART (X²= 2.315, df= 4, P-value= 0.678).

Table 3.23: Age groups versus Adherence status Cross-tabulation

			Adherence status		Total
			Poor	Good	
Age groups	Age group younger than 30 years old	Count	9	6	15
		% within Age groups	60.0%	40.0%	100.0%
		% within Adherence status	15.0%	10.5%	12.8%
		% of Total	7.7%	5.1%	12.8%
	Age group 30-34 years old	Count	14	13	27
		% within Age groups	51.9%	48.1%	100.0%
		% within Adherence status	23.3%	22.8%	23.1%
		% of Total	12.0%	11.1%	23.1%
	Age group 35-39 years old	Count	14	14	28
		% within Age groups	50.0%	50.0%	100.0%
		% within Adherence status	23.3%	24.6%	23.9%
		% of Total	12.0%	12.0%	23.9%
	Age group 40-44 years old	Count	9	14	23
		% within Age groups	39.1%	60.9%	100.0%
		% within Adherence status	15.0%	24.6%	19.7%
		% of Total	7.7%	12.0%	19.7%
	Age group older than 44 years old	Count	14	10	24
		% within Age groups	58.3%	41.7%	100.0%
		% within Adherence status	23.3%	17.5%	20.5%
		% of Total	12.0%	8.5%	20.5%
Total		Count	60	57	117
		% within Age groups	51.3%	48.7%	100.0%
		% within Adherence status	100.0%	100.0%	100.0%
		% of Total	51.3%	48.7%	100.0%

3.3.2.3. Results of association between CD4 groups and adherence to ART

analysis

Table 3.24: CD4 groups versus adherence status cross-tabulation

			Adherence status		Total
			Poor	Good	
CD4 groups	CD4 group1-99	Count	33	33	66
		% within CD4 groups	50.0%	50.0%	100.0%
		% within Adherence status	55.0%	57.9%	56.4%
		% of Total	28.2%	28.2%	56.4%
	CD4 group 100-199	Count	11	11	22
		% within CD4 groups	50.0%	50.0%	100.0%
		% within Adherence status	18.3%	19.3%	18.8%
		% of Total	9.4%	9.4%	18.8%
	CD4 greater than 199	Count	16	13	29
		% within CD4 groups	55.2%	44.8%	100.0%
		% within Adherence status	26.7%	22.8%	24.8%
		% of Total	13.7%	11.1%	24.8%
Total		Count	60	57	117
		% within CD4 groups	51.3%	48.7%	100.0%
		% within Adherence status	100.0%	100.0%	100.0%
		% of Total	51.3%	48.7%	100.0%

This table demonstrates that the majority of all the research respondents, 56.4 percent, had CD4 group 1-99. Poor and good adherent patients, nonetheless, accounted for the same number, 33. Likewise, of the 29 patients, who have CD4 group greater than 199, the number of poor and good adherent patients was almost the same. In this context, no statistically significant association between CD4 groups and adherence to ART was found at all (X^2=0.234, df= 2, P-value= 0.890).

3.3.2.4. Results of association between WHO stages and adherence to ART analysis

Table 3.25: WHO stage versus adherence status cross-tabulation

			Adherence status		Total
			Poor	Good	
WHO stage	WHO stage 1	Count	6	1	7
		% within WHO stage	85.7%	14.3%	100.0%
		% within Adherence status	10.0%	1.8%	6.0%
		% of Total	5.1%	.9%	6.0%
	WHO stage 2	Count	9	8	17
		% within WHO stage	52.9%	47.1%	100.0%
		% within Adherence status	15.0%	14.0%	14.5%
		% of Total	7.7%	6.8%	14.5%
	WHO stage 3	Count	24	28	52
		% within WHO stage	46.2%	53.8%	100.0%
		% within Adherence status	40.0%	49.1%	44.4%
		% of Total	20.5%	23.9%	44.4%
	WHO stage 4	Count	21	20	41
		% within WHO stage	51.2%	48.8%	100.0%
		% within Adherence status	35.0%	35.1%	35.0%
		% of Total	17.9%	17.1%	35.0%
Total		Count	60	57	117
		% within WHO stage	51.3%	48.7%	100.0%
		% within Adherence status	100.0%	100.0%	100.0%
		% of Total	51.3%	48.7%	100.0%

This table illustrates that the number of HIV/AIDS patients with WHO stages 3 and 4 was 44.4 and 35 percent, respectively. Of the WHO stage 4 subjects, poor and good adherent patients accounted for nearly the same. The number of poor and good adherent patients in WHO stage 3 was slightly different. Even so, there is no statistically significant association between WHO stages and adherence to ART (X^2= 3.888, df= 3, P-value= 0.274).

3.3.2.5. Results of Association between Marital Status and Adherence to ART Analysis

Table 3.26: Marital status versus adherence status cross-tabulation

			Adherence status		Total
			Poor	Good	
Marital status	Single	Count	3	5	8
		% within Marital status	37.5%	62.5%	100.0%
		% within Adherence status	5.0%	8.8%	6.8%
		% of Total	2.6%	4.3%	6.8%
	Married	Count	37	32	69
		% within Marital status	53.6%	46.4%	100.0%
		% within Adherence status	61.7%	56.1%	59.0%
		% of Total	31.6%	27.4%	59.0%
	Divorced	Count	13	11	24
		% within Marital status	54.2%	45.8%	100.0%
		% within Adherence status	21.7%	19.3%	20.5%
		% of Total	11.1%	9.4%	20.5%
	Others	Count	7	9	16
		% within Marital status	43.8%	56.3%	100.0%
		% within Adherence status	11.7%	15.8%	13.7%
		% of Total	6.0%	7.7%	13.7%
	Total	Count	60	57	117
		% within Marital status	51.3%	48.7%	100.0%
		% within Adherence status	100.0%	100.0%	100.0%
		% of Total	51.3%	48.7%	100.0%

This table shows that the majority of all research respondents (59 percent) were married. However, there was not a big difference between numbers of poor and good adherent patients. Among the 24 patients who were divorced, the number of poor adherent and good adherent patients was similar. In addition, there is no statistically significant association between marital status and adherence to ART

119

(X²= 5.289, df= 5, P-value= 0.382).

3.3.2.6. Results of association between occupation and adherence to ART Analysis

Table 3.27: Occupation versus adherence status cross-tabulation

			Adherence status		Total
			Poor	Good	
Occupations	Unemployed	Count	12	15	27
		% within Occupation	44.4%	55.6%	100.0%
		% within Adherence status	20.0%	26.3%	23.1%
		% of Total	10.3%	12.8%	23.1%
	Farmer	Count	5	2	7
		% within Occupation	71.4%	28.6%	100.0%
		% within Adherence status	8.3%	3.5%	6.0%
		% of Total	4.3%	1.7%	6.0%
	Civil servant	Count	3	10	13
		% within Occupation	23.1%	76.9%	100.0%
		% within Adherence status	5.0%	17.5%	11.1%
		% of Total	2.6%	8.5%	11.1%
	Small business/self employed	Count	16	15	31
		% within Occupation	51.6%	48.4%	100.0%
		% within Adherence status	26.7%	26.3%	26.5%
		% of Total	13.7%	12.8%	26.5%
	Company worker	Count	17	8	25
		% within Occupation	68.0%	32.0%	100.0%
		% within Adherence status	28.3%	14.0%	21.4%
		% of Total	14.5%	6.8%	21.4%
	Others	Count	7	7	14
		% within Occupation	50.0%	50.0%	100.0%
		% within Adherence status	11.7%	12.3%	12.0%
		% of Total	6.0%	6.0%	12.0%
	Total	Count	60	57	117
		% within Occupation	51.3%	48.7%	100.0%
		% within Adherence status	100.0%	100.0%	100.0%
		% of Total	51.3%	48.7%	100.0%

This table shows that the number of small business/self-employed patients is greater than that of the other occupations. Of the 31 (26.5%), however, the number of poor and good adherent patients was almost the same, 16 versus 15. Among the 25 patients who are unemployed, 12 were poor adherent and 15 good adherent patients. Moreover, company workers, third range from small business/self-employed patients, accounted for 25, of whom 17 were poor adherent, while eight were good adherent patients. As can be seen in the table, there is a big difference between the numbers of poor and good adherent patients in the company worker occupation. Farmers, in contrast, have the smallest number among all the occupations. Though there are some similarities and differences between the numbers of poor and good adherent patients, there is no statistically significant association between occupations and adherence to ART (X^2= 8.589, df= 5, P-value= 0.127).

3.3.2.7. Results of association between food and adherence to ART analysis

Table 3.28 demonstrates that 60 (51.3%) and 57 (48.7%) of the entire 117 sample, were poor and good adherent patients, respectively. The majority of all the research respondents, 68 (58.1%) had enough food to eat every day, while 49 (49.1%) did not have it. Although about 49 percent of all the patients who participated in the study did not have enough food to eat every day, this number is higher than the poverty rate in Cambodia, which is about 35 percent of the total population. Even though a difference between enough and not enough food to eat daily is found, there is no statistically significant association between food and

adherence to ART (X²= 0.179, df= 1, P-value= 0.672).

Table 3.28: Food status versus adherence status cross-tabulation

| | | | Adherence status | | |
			Poor	Good	Total
Food status	Enough	Count	36	32	68
		% within Food status	52.9%	47.1%	100.0%
		% within Adherence status	60.0%	56.1%	58.1%
		% of Total	30.8%	27.4%	58.1%
	Not enough	Count	24	25	49
		% within Food status	49.0%	51.0%	100.0%
		% within Adherence status	40.0%	43.9%	41.9%
		% of Total	20.5%	21.4%	41.9%
Total		Count	60	57	117
		% within Food status	51.3%	48.7%	100.0%
		% within Adherence status	100.0%	100.0%	100.0%
		% of Total	51.3%	48.7%	100.0%

3.4. Chapter summary

The results presented above indicate clearly that there are 60 and 57 poor and good adherent patients out of the entire sample 117, and most of the study subjects experienced side effects of ART. The study focuses on looking for barriers to antiretroviral therapy adherence of HIV/AIDS patients at Sihanouk Hospital Center of HOPE, Phnom Penh, Cambodia.

Table 3.29 presents the results of association between socio-demographic and economic factors other than those included in the hypothesis testing and adherence to ART analyses. There are four columns in the table; the first represents variables of study, second Chi-square test values, third degree of freedom (DF), and last column P-value. As can be seen in the table, socio-demographic and economic factors such as

gender, age groups, and CD4 groups are not statistically significantly associated with adherence to ART since all the P-values are greater than 0.05 (α-level).

Table 3.29: Summary of Chi-square test of association between socio-economic factors and adherence to ART

Variables	Chi-square value (X^2)	DF	-value
Gender vs adherence to ART	1.235	1	0.266
Age groups vs adherence to ART	2.315	4	0.678
CD4 groups vs adherence to ART	0.234	2	0.89
WHO stages vs adherence to ART	3.888	3	0.274
Marital status vs adherence to ART	5.289	5	0.382
Occupations vs adherence to ART	8.589	5	0.127
Food status vs adherence to ART	0.179	1	0.672

Table 3.30 shows the results of hypothesis testing. This table has four columns, of which each represents the same elements as those of table 3.29. ART side effects are the only one out of the seven hypothesis testing variables that is statistically significantly associated with adherence to ART (P-value= 0.007). In addition, of all the side effects that most HIV/AIDS patients experienced, gastro-intestinal side effects such as nausea, vomiting, and abdominal pain, are specifically the only ones which have a significant association with adherence to ART (P-value= 0.002).

Table 3.30: Summary of Chi-square test of association of hypothesis testing

Variables	Chi-square value (X^2)	DF	P-value
ART regimens vs adherence to ART	0.165	1	0.685
OI drug uses vs adherence to ART	0.29	1	0.865
Knowledge of ART vs adherence to ART	0.009	1	0.925
Educational levels vs adherence to ART	3.555	3	0.314
Patient's address vs adherence to ART	0.28	1	0.868
Poverty vs adherence to ART	0	1	0.983
Side effects vs adherence to ART	7.15	1	0.007
Gastro-intestinal side effects vs adherence to ART	9.535	1	0.002

Therefore, the barriers to antiretroviral therapy adherence of the HIV/AIDS patients are mainly the ART side effects of which only gastro-intestinal side effects are statistically significantly associated with poor ART adherence.

A more detailed summary and discussions of the findings are presented in the next chapter.

CHAPTER IV: SUMMARY, DISCUSSIONS, CONCLUSIONS, POLICY IMPLICATIONS, AND SUGGESTION FOR FUTURE RESEARCH

This chapter is divided into five sections. First, the summary section provides statement of research problems and reviews major methods used in this study. Second, the discussion section summarizes and compares findings with those of previous research in accordance with research objectives, research questions, and research hypotheses. Third, the conclusion section draws conclusions from discussion section and overall contents of the study in relation to research objectives. Fourth, the policy implication section provides comprehensive interventions and recommendations to stakeholders for improving ART adherence. Last, the suggestion for future research section seeks to fill up the gaps in the study.

4.1. Summary

Adherence to antiretroviral therapy is a global problem, especially in poor-resource setting countries such Cambodia as an example. This study was conducted to identify barriers to antiretroviral therapy adherence of HIV/AIDS patients at Sihanouk Hospital Center of HOPE between August 16, 2010 and September 30, 2010. The study design is a cross-sectional survey in the form of a case-control study of poor ART adherent patients and good ART adherent patients, which employed both quantitative and qualitative approaches. Purposive and simple random sampling techniques were used in the study for recruiting poor ART adherent patients and good ART adherent patients, respectively.

Primary data were collected using face-to-face interviews through a self-administered and structured questionnaire. While secondary data were collected using cohort data in order to identify poor ART adherent patients and good ART adherent patients among all HIV/AIDS patients who were on highly active antiretroviral therapy (HARRT) through a visual analogue scale at the Infectious Disease Department of Sihanouk Hospital Center of HOPE. Also, the secondary data were collected through a variety of other sources in a bid to find out relevant documents, information, and previous research findings.

In total, 117 subjects were recruited in the study, 60 of whom were poor ART adherent patients, and 57 good ART adherent patients. The author had a list of these poor and good ART adherent patients before the interviews. Furthermore, data were coded and analyzed using SPSS version 18, and Chi-square test was used to identify the association between dependent and independent categorical variables. Results of data analysis show that the majority (93%) of the total 117 research respondents are good ART adherent patients, while seven percent are poor ART adherent patients.

4.2. Discussions

The results of analysis were discussed following three main parts: results of reasons reported for missing ART doses in this study, results of hypothesis testing, and results of socio-demographic and economic factors.

4.2.1. Discussions on results of reasons reported for missing ART doses in this study

When asked (do you take ARVs regularly, continuously, and correctly?), 47 percent of all research subjects said that they took their ARVs correctly, while 53 percent said that they took their ARVs incorrectly. This question was asked in order to know whether or not patients take ARVs correctly. The question did not focus on patients' taking their ARVs in the last month before the interviews; however, it intended to get general information on ART adherence and seems to be true according to their answers since they have taken ARVs by the time of interviews. This result is similar to previous research findings (Paterson et al., 2002; World Health Organization, 2003; Steel, Nwokike & Joshi, 2007).

Most of the patients who took ARVs correctly said that alarm clock, reminders of family, relatives, and friends, along with high commitment, were the key factors for taking ARVs correctly. These answers may be reasonable and acceptable in their daily routine and practice. They are also consistent with previous research findings (Machtinger & Bangsberg, 2006; Huong, 2009). Among those who took ARVs incorrectly, the reasons for missing medication doses were forgetfulness (22.2%), being busy, conflicts with family and neighbors, lacks of time reminders such as alarm clock and cell phone, which altogether contributed to 35.9%, too ill (6%), fear of stigma/disclosure (6%), drunk with alcohol (5.1%), felt better (2.6%), developed toxicity/side effects (2.6%), too many pills/pill burden (2.6%), or stock was finished (1.7%). These results are likely true and similar to previous research

findings (Hardon et al, 2006; Markos, Worku, & Davey, 2008; Wanjohi, 2009). Furthermore, when asked (many people find it hard to remember to take every single dose; how many doses of ARVs in the last month prior to interview have you missed?), the majority of research respondents 106 (90.6%) did not miss their doses, while 11 (9.4%) missed their doses. Eight (about 73%) of 11 respondents missed ART more than three doses during one month before the interview. This equaled about seven percent of all research respondents that are poor ART adherent patients. The percentage of poor ART adherent patients (about 7%) in this study is higher than the percentage of poor ART adherent patients (about 3%) of all 2467 HIV/AIDS patients who were on ART since the beginning of ART program until March 2010 at Sihanouk Hospital Center of HOPE. This finding seems to be true because when interviewing respondents, the author used the questionnaire, which was prepared and organized in detail in order to seek for answers and information in accordance with the study objectives. Another possibility is that patients so far might have over-reported ART adherence to physicians and counselors fearing of being blamed by health care providers if they tell their real ART adherence. Therefore, most of the research respondents (93%) in this study are good ART adherent patients, while eight (7%) are poor ART adherent patients. The percentage of poor adherence in this study is much lower than that of some previous studies as follows: Ethiopia, 26% (Markos, Worku & Davey, 2008), Kenya, 26% (Wanjohi, 2009), and Vietnam, 37% (Huong, 2009). Also, the percentage of poor ART adherent patients (7%) is lower than that in the national level (13%) (NAA, 2007) and even lower than the percentage of poor

ART adherent patients at Calmette Hospital (29%) (Olivier et al., 2010). This study has a lower level of poor ART adherence (7%) than that in other studies, possibly due to the fact that Sihanouk Hospital Center of HOPE provides free health care services to HIV/AIDS patients. Besides, health care staff of the hospital has probably the highest capacity of taking care, treatment, support, and management of HIV/AIDS patients in the country.

4.2.2. Results of hypothesis testing

There are seven hypotheses in this research:

- ART side effects may influence adherence to ART.

- ART regimens may influence adherence to ART.

- Co-opportunistic infection treatment drugs may influence adherence to ART.

- Levels of patient knowledge of ART may influence adherence to ART.

- Educational levels of patients may influence adherence to ART.

- Patient's location of residence may influence adherence to ART

- Poverty status of patients may influence adherence to ART.

4.2.2.1. ART side effects may influence adherence to ART

Results show that 83 (70.94%) of the total research respondents experienced side effects of which 43.4% were poor ART adherent patients. Among 34 patients who did not experience side effects, 24 (70.6%) were poor ART adherent patients. Out of 83 patients who experienced side effects, only about 13 percent experienced

adverse effects to the extent of stopping the medicines. However, the results of analysis show that ART side effects are statistically significantly associated with adherence to antiretroviral therapy (X^2=7.150, df =1, P-value=0.007). It might be due to subjective answers of patients or patients might not know that these symptoms are ART side effects; or patients might have been accustomed to adverse effects of medications due to the physical and emotional morbidity or well-being related to patients. The significant association between ART side effects and adherence to antiretroviral therapy in this study is consistent with previous research findings (Ickovics & Meade, 2002; Castro 2005; Markos, Worku, & Davey, 2008; Cauldbeck, et al., 2009). Furthermore, in this study gastro-intestinal problems are the only one ART side effects that are statistically significantly associated with ART adherence (X^2= 9.535, df = 1, P-value= 0.002). This association is also found in previous studies (Markos, Worku, & Davey, 2008; Cauldbeck, et al., 2009). The possibility that gastro-intestinal side effects, such as nausea, vomiting, abdominal discomfort as well as pain, and diarrhea, influence poor adherence is because these symptoms are the most common after patients take their ARVs and that can influence their daily routine. The gastro-intestinal side effects including nausea, vomiting, and abdominal pain are mainly caused by Nucleoside Reverse Transcriptase Inhibitors (NRTIs) such as AZT and D4T and diarrhea is due to Protease Inhibitors (PIs) such as KALETRA (Sihanouk Hospital Center of HOPE, 2008).

4.2.2.2. ART Regimens may influence adherence to ART

At Sihanouk Hospital Center of HOPE (SHCH) and in Cambodia, there are only two ART line regimens, first line and second-line ART regimens. First-line ART regimen consists of seven regimens such as 3TC+EFV+AZT, 3TC+EFV+TDF, 3TC+NVP+AZT, 3TC+NVP+TDF, ABC+3TC+EFV, D4T+3TC+EFV, and D4T+3TC+NVP, while second-line ART regimen is composed of four regimens such as 3TC+TDF+KALETRA, 3TC+TDF+KALETRA+AZT, ABC+DDI+KALETRA, and D4T+3TC+KALETRA. The majority 106 (90.6%) of the total 117 patients are on first-line ART regimens, while 11 (9.4%) patients are on second-line ART regimens. Among 106 patients, who are on first-line ART, 55 and 51 patients belong to poor adherent and good adherent patient groups, respectively. As for 11 patients, who are on second-line ART, five and six patients belong to poor adherent and good adherent patients, respectively. The number of poor ART adherent and good ART adherent patients on first-line ART was almost the same. Similarly, the number of poor ART adherent and good ART adherent patients on second-line ART was almost the same. Results show that both first-line and second-line ART regimens were not statistically significantly associated with adherence status (poor and good adherence) (X^2= 0.165, df = 1, P-value= 0.685). This may be because almost all patients were on first-line ART, which has fewer pills than second-line ART or the number of poor ART adherent and good ART adherent is nearly the same or patients were well trained and educated about antiretroviral therapy or the way that patients take medications in their daily routine. Another possible explanation could be that both first-line ART

regimens and second-line ART regimens had worse side effects as just mentioned above. Previous studies have found similar results in favor of the results of this study (Markos, Worku, & Davey, 2008; Cauldbeck et al., 2009). However, Nemes, Carvalho and Souza (2004) and Wanjohi (2009) found that ART regimens were statistically significantly associated with adherence to antiretroviral therapy.

4.2.2.3. Co-opportunistic infection treatment drugs may influence adherence to ART

The majority 102 (87.2%) of the patients took OI drugs, while 15 (12.8%) did not take them. Among 102 patients who took drugs, 50 were good ART adherent patients, while 52 were poor ART adherent patients. Moreover, among 15 patients who did not take drugs, eight were poor ART adherent patients, while seven good ART patients. Results of this study show that co-treatments of opportunistic infections (OI), regardless of numbers of time (frequency) of taking drugs and numbers of drugs taken, were not significantly associated with adherence to antiretroviral therapy ($X^2 = 0.29$, df = 1, P value= 0.865). These results are consistent with patients' answers to a question asked (do you have difficulty taking ARVs while concomitantly taking OI drugs?). 83% of 102 patients who took OI drugs said that they did not have difficulty taking ARVs while taking other drugs. It might be due to their daily routine of taking drugs, or most of the regimens were first-line ART or there were no drug-drug interaction, or maybe patients were aware of benefits of antiretroviral therapy, especially it may be due to their high commitment of taking drugs in order to improve their quality of life. Other previous research findings found

that ART regimens and co-treatment of OI drugs were not significantly associated with adherence to antiretroviral therapy (Markos, Worku, & Davey 2008; Zungu, 2009; Cauldbeck et al., 2009). On the contrary, Wanjohi (2009) reported that co-treatment of HIV and other infections were significantly associated with adherence.

4.2.2.4. Levels of patient knowledge of ART may influence adherence to ART

105 (89.7%) and 12 (10.3%) of the total 117 patients showed high knowledge and low knowledge of antiretroviral therapy, respectively. Of the 105 patients who had high knowledge of ART, 54 were poor ART adherent patients, while 51 good ART adherent patients. Among 12 patients who had low knowledge of ART, six were poor ART adherent patients and another six were good ART adherent patients. Results of analysis show that levels of patient knowledge of ART were not statistically significantly associated with adherence to antiretroviral therapy (X^2= 0.009, df =1, P-value= 0.925). Patients with high knowledge of ART may owe it to the results of hospital education and training by physicians, counselors, and also they can learn from their peers. However, despite high knowledge of ART, some patients do not perform good attitude and practice towards good adherence at all. These results are concordant with other previous research findings (Markos, Worku, & Davey, 2008; Cauldbeck et al., 2009).

4.2.2.5. Educational levels of patients may influence adherence to ART

Educational backgrounds of research subjects in this study were divided into four levels: illiterate 31 (26.5%), primary school 40 (34.2%), secondary school 27

(23.1%), and high school or university 19 (16.2%). It is seen in the findings chapter that among 117 respondents, the number of patients attending primary school is the highest, followed by illiterate, secondary school, and high school or university. In illiterate level, there were 31 patients; of these, 19 were poor adherent patients, while 12 good adherent patients. Next, in primary school level, of the 40 patients, 22 and 18 were poor ART adherent and good ART adherent patients, respectively. Among 27 patients in secondary school level, 12 were poor ART adherent patients, while 15 good ART adherent patients. Furthermore, of the 19 patients in high school or university level, seven were poor ART adherent patients, while 12 good ART adherent patients. Even though there is a difference between the numbers of poor and good ART adherent patients in each level of education, results of analysis show that there is no statistically significant association between educational levels and adherence to antiretroviral therapy (X^2= 3.555, df= 3, P-value= 0.314). It seems likely that patients may have poor adherence to antiretroviral therapy when their educational background is low; however, high educational background seems to be a predictor of good adherence. In contrast, in this study education regardless of levels of study was not significantly associated with ART adherence. This might be because of poor attitude and practice. The results of this study are relevant to other research findings (Markos, Worku, & Davey, 2008; Cauldbeck et al., 2009). However, some previous research findings contrast with this study (Nemes, Carvalho & Souza, 2004; Wanjohi, 2009).

4.2.2.6. Patient's location of residence may influence adherence to ART

73 (62.4%) of all research respondents live in Phnom Penh, while 44 (37.6%) live in provinces. 37 out of 73 patients who live in Phnom Penh were poor ART adherent patients, while 36 were good ART adherent patients. Among 44 research respondents who live in provinces, 23 were poor ART adherent patients, while 21 were good ART adherent patients. Apparently, there is almost the same number of poor and good adherent patients living in Phnom Penh, and also the number of poor and good adherent patients living in provinces. Results of analysis demonstrate that patient's location of residence has no significant association with adherence to antiretroviral therapy (X^2=0.28, df =1, P-value= 0.868). This may be due to almost no difference between the number of poor adherent patients and good adherent patients in both sites. Some might think that when living far away from health facility, patients seem to perform poor ART adherence because of the cost and time spent on transportation, foods, and difficult access to health facilities. Some previous study findings are consistent with the results of this study (Hardon et al, 2006; Cauldbeck et al., 2009). On the contrary, one previous research finding found that living away from home was significantly associated with poor adherence (Markos, Worku, & Davey, 2008).

4.2.2.7. Poverty status of patients may influence adherence to ART

82 (70.1%) of the 117 research subjects were poor, while 35 (29.9%) were not poor. However, there was almost no difference between the number of poor ART adherent patients (42) and good ART adherent patients among all poor patients (40).

Similarly, of the 35 patients who were not poor, 18 were poor ART adherent patients, while 17 are good ART adherent patients. There is no statistically significant association between poverty status and adherence to antiretroviral therapy (X^2=0.000, df =1, P value=0.983). This might be due to almost the same numbers of poor ART adherent patients and good ART adherent patients in poor and not poor patients' groups or it seems that poor patients might have high commitment to take ARVs in order to improve their quality of life because they cannot afford to buy drugs by themselves. This finding is consistent with other previous findings (Orrell, Bangsberga, Badri, & Wood, 2003; Cauldbeck et al., 2009). In contrast, some previous studies found that poverty is statistically significantly associated with poor ART adherence (Nemes, Carvalho & Souza, 2004; Machtinger & Bangsberg, 2006; Wanjohi, 2009).

4.2.3. Results of socio-demographic and economic factors

There are seven socio-demographic and economic factors: gender, age groups, CD4 groups, WHO stages, marital status, occupations, and food access status.

4.2.3.1. Gender

45 (38.5%) of all research respondents were males, while 72 (61.5%) were females. Among 45 male patients, 26 were poor ART adherent patients, while 19 are good ART adherent patients. 34 of 72 female patients were poor ART adherent patiernts, while 38 were good ART adherent patients. Results of the analysis show that there is no statitistically significant association between gender and adherence to

antiretroviral therapy (X²= 1.235, df = 1, P-value=0.266). This result is supported by previous research findings (Orrell, Bangsberga, Badri, & Wood, 2003, Erah, & Arute, 2008). However, some previous study findings showed that gender is associated with ART adherence (Shernoff, 2001; Kennedy, Goggin, & Nollen, 2004; Cauldbeck et al., 2009).

4.2.3.2. Age groups

As mentioned in chapter III, age groups are classified into five categories. Age groups 30-34 and 35-39 years had greater numbers than those in other age groups. These two groups account for 23.1 and 23.9%, respectively. Results of analysis reveal that age groups were not associated with ART adherence (X²= 2.315, df= 4, P-value= 0.678). This result is consistent with previous research findings (Nemes, Carvalho & Souza, 2004; Erah & Arute, 2008). On the contrary, other previous research findings revealed that age groups were associated with ART adherence (Nemes, Carvalho & Souza, 2004; Machtinger & Bangsberg, 2006; Wanjohi, 2009; Cauldbeck et al., 2009).

4.2.3.3. CD4 groups

As seen in the findings chapter, CD4 groups were divided into three categories. Of these, CD4 group 1-99 accounted for the majority (56.4%). However, of all patients (66) in this CD4 group, the numbers of poor and good ART adherent patients are the same (33). Similarly, the numbers of poor ART adherent patients and good ART adherent patients in the other two CD4 groups are almost the same.

Results of analysis indicate that CD4 groups were not statistically significantly associated with adherence to antiretroviral therapy. ART adherence might be influenced by other factors, for example, ART side effects, other than CD4. Other findings are in favor of this result (Erah & Arute, 2008; Ford, Darder, Spelman, Maclean, Mills, & Boulle, 2010). In contrast, previous research findings demonstrated that CD4 is statistically significantly associated with ART adherence (Wood, Hogg, Yip, Harrigan, O'Shaughnessy, & Montaner, 2003; Machtinger & Bangsberg, 2006).

4.2.3.4. WHO stages

Among all the research respondents, WHO stage 3 and WHO stage 4 accounts for 44.4% and 35%, respectively. While the other stages represent the minority. Among seven respondents in WHO stage 1, six are poor ART adherent patients, while one is good ART adherent patient. However, the numbers of poor ART adherent and good ART adherent patients in WHO stage 2 are almost the same, nine and eight, respectively. Among 52 respondents in WHO stage 3, 24 are poor ART adherent patients, while 28 are good ART adherent patients. This shows a slight difference between the numbers of poor and good ART adherent patients. However, of all 41 respondents in WHO stage 4, the numbers of poor and good ART adherent patients were almost the same, 21 and 20, respectively. Results of analysis show that WHO stages were not significantly associated with ART adherence ($X^2= 3.888$, df= 3, P-value= 0.274). ART might be influenced by other factors such complex ART

regimens, socio-demographic characteristics, and disease factors. This result is consistent with some previous research findings (Orrell, Bangsberga, Badri, & Wood, 2003; Bajunirwe, Arts, Tisch, King, Debanne, & Sethi, 2009). However, it is in contrast with previous research findings (Wood, Hogg, Yip, Harrigan, O'Shaughnessy, & Montaner, 2003; Cauldbeck et al., 2009).

4.2.3.5. Marital status

As shown in findings chapter, the majority (59%) of the respondents were married, followed by divorced (20.5%). The remaining marital status categories represent the minority. Among 69 married respondents, 37 were poor ART adherent patients, while 32 were good ART adherent patients. Of the 24 divorced respondents, 13 were poor ART adherent patients, while 11 were good ART adherent patients. Results of analysis demonstrate that marital status was not statistically significantly associated with adherence to antiretroviral therapy (X^2= 5.289, df= 5, P-value = 0.382). This result is compatible with previous research findings (Orrell, Bangsberga, Badri, & Wood, 2003; Huong, 2009; Bajunirwe, Arts, Tisch, King, Debanne, & Sethi, 2009)**.** However, this result is not consistent with some other previous research findings (Nemes, Carvalho, & Souza, 2004; Machtinger & Bangsberg, 2006; Wanjohi, 2009).

4.2.3.6. Occupations

As described in findings chapter, the numbers of respondents who had a small business, were unemployed, and company workers accounted for 31 (26.5%), 27

(23.1%), 25 (21.4%), respectively. While the other occupation categories represent the minority. 16 of 31 respondents, who had small business or were self-employed, were poor ART adherent patients, while 15 were good ART adherent patients. Among 27 unemployed, 12 were poor ART adherent patients, while 15 were good ART adherent patients. 17 out of 25 company workers were poor ART adherent patients, while eight were good ART adherent patients. Results of analysis show that occupations were not significantly associated with ART adherence. Previous research findings are in favor of this result (Orrell, Bangsberga, Badri, & Wood, 2003; Markos, Worku, & Davey, 2008). However, findings of some previous studies are against this result (Nemes, Carvalho, & Souza, 2004; Machtinger & Bangsberg, 2006; Wanjohi, 2009; Huong, 2009).

4.2.3.7. Food access status

68 (58.1%) and 49 (49.1%) of all research respondents have enough and do not have enough food to eat every day, respectively. 36 out of 68 respondents who had enough food to eat were poor ART adherent patients, while 32 were good ART adherent patients. Among 49 respondents who did not have enough food to eat every day, 24 were poor ART adherent patients, while 25 were good ART adherent patients. Although about 49 percent of all the patients who participated in the study did not have enough food to eat every day, this number is higher than poverty rate in Cambodia, which is about 35 percent of the total population. Results of analysis in this study demonstrate that food access was not statistically significantly associated

with adherence to antiretroviral therapy (X²= 0.179, df = 1, P-value= 0.672). This result is in agreement with one previous research finding (Manary, Ndekha, & Oosterhout, 2010). However, this result is consistent with previous research findings (Nemes, Carvalho, & Souza, 2004; Machtinger & Bangsberg, 2006; Huong, 2009; Wanjohi, 2009).

4.3. Conclusions

Cambodia is one of the developing countries that have been hit by HIV/AIDS epidemic and many AIDS patients have died of this disease. In order to contain the epidemic and reduce the morbidity and mortality related to HIV/AIDS, the Royal Government of Cambodia, along with civil societies, local and international organizations, and other stakeholders, has co-operated and worked together to prevent HIV transmission, provide patients with care, treatment, support, and other related managements. Moreover, antiretroviral therapy coverage has been expanded and increased rapidly in order to meet the demands of HIV/AIDS patients. ART program in Cambodia has been successful and has reduced HIV prevalence, morbidity and mortality and burdens related to the disease dramatically. Also, the effectiveness of ART program has improved the quality of life of HIV/AIDS patients substantially. Because the number of people living with HIV/AIDS needing ART has increased rapidly, appropriate measures need to be taken thoroughly and carefully in order to achieve long-term success. Adherence to antiretroviral therapy is one of the key factors that contribute to the effectiveness and success of antiretroviral therapy and it

needs to be optimal, otherwise the success of treatment cannot be achieved. Adherence to ART faces many problems; however, there has been so far nearly no study on problems that can lead to poor ART adherence in Cambodia. Hence, the author chose to study barriers to antiretroviral therapy adherence of HIV/AIDS patients at Sihanouk Hospital Center of HOPE, Phnom Penh, Cambodia.

The findings of the study show that the majority of all research respondents (93%) were good ART adherent patients, whereas seven percent were poor ART adherent patients. The main factors for good ART adherence cited by research respondents are access to alarm clock, reminders of family, relatives, and friends, as well as high commitment of patients. The reasons for poor ART adherence also reported by research respondents are forgetfulness, being busy, lack of time reminders, seriousness of diseases, stigma/discrimination, ART side effects, and high pill burdens. Univariate data analysis shows that ART side effects are the only one factor of the other hypotheses that is statistically significantly associated with poor ART adherence (X^2=7.150, df =1, P-value =0.007). Exclusively, of all ART side effects, gastro-intestinal symptoms were the only one factor that is statistically significantly associated with poor ART adherence (X^2= 9.535, df= 1, P-value= 0.002). The other hypotheses such as ART regimens, co-opportunistic infection drug treatments, knowledge of ART, educational levels, patient's location of residence, and poverty status are not significantly associated with poor ART adherence. Other

factors such as gender, age groups, CD4 groups, WHO stages, marital status, occupations, and food status are not significant predictors for poor ART adherence.

Therefore, the significant barriers to adherence to antiretroviral therapy adherence of the HIV/AIDS patients at Sihanouk Hospital Center of HOPE are side effects of antiretroviral treatments. Other factors such as forgetfulness, being busy, lack of time reminders, seriousness of disease, social and cultural factors such as stigma and discrimination are also predictors of poor adherence to antiretroviral therapy.

4.4. Policy implications

Based on discussions and conclusions above, levels of adherence to antiretroviral therapy of HIV/AIDS patients at Sihanouk Hospital Center of HOPE and in Cambodia are generally good; however, poor ART adherence still exists and needs to be addressed by stakeholders including people who are responsible for ART program and those working for relevant governmental and non-governmental institutions. Therefore, in order to improve adherence to antiretroviral therapy of HIV/AIDS patients in Cambodia, the implication of comprehensive interventions is needed and some recommendations can be considered and made as follows:

- ART programs should provide clinicians with more education and training on antiretroviral therapy and management of ART side effects. The programs could also train counselors to educate and counsel HIV/AIDS patients to improve their ART adherence during hospital visits and other

activities. Doctors should closely observe and manage ART side effects including nausea, vomiting, abdominal pain, and diarrhea. In case that the adverse effects are worsening or remains permanent, they may change the most likely drugs.

- Physicians, nurses, pharmacists, counselors, and home-based care workers need to work as a team in order to achieve a common goal of ART success. For that reason, they need to educate and train HIV/AIDS patients to understand the benefits and goal of antiretroviral therapy appropriately. Most importantly, physicians should explain deeply, thoroughly, and well in advance to patients that ART side effects may occur after they take antiretroviral drugs. Moreover, doctors should educate and train HIV/AIDS patients to understand and recognize adverse effects of ART and ask the patients to inform them in case that ART side effects happen or doctors should tell patients to go to hospital for side effect management.

- The Ministry of Health of Cambodia could improve and strengthen quality of HIV/AIDS disease treatment and management, especially ART side effects of clinicians, nurses, pharmacists, and counselors who are working in ART sites in the country as a whole. Moreover, the Ministry of Health could consider policy on program switching ARV drugs that are most likely to cause side effects such as nausea, vomiting, abdominal pain, and

diarrhea or if possible, the Ministry of Health could provide alternatives of ARV drugs that can avoid gastro-intestinal adverse effects.

- The Royal government of Cambodia through the Ministry of Health, authority/community, civil society, non-governmental organizations (NGO), and other involved ministries should work together so as to intensify health education campaigns against stigma and discrimination, provide more job opportunity, promote family and community support for HIV/AIDS patients, and to provide patients with time reminders such as alarm clock.

The findings of this study would be important for ART program managers and policy makers to improve the success of antiretroviral therapy. Thus, the Cambodian government can have the best opportunity to save more money and contribute to country development.

4.5. Suggestion for future research

- Studies on a bigger sample and using mixed methods including subjective self-report and objective pill count to assess adherence to antiretroviral therapy of people living with HIV/AIDS should be conducted.

- Studies on ART adherence should focus on both HIV/AIDS patients and health care providers in order to produce more reliable and accurate results.

- Studies should be conducted in more than one setting and need to be compared with other settings in urban and rural areas.

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APPENDICES

Appendix 1: Consent form

My name is HING Kim. I am a Master of Public Health Management student at the Ritsumeikan Asia Pacific University, Japan. I am conducting a survey on "Barriers to Antiretroviral Therapy Adherence of HIV/AIDS Patients at Sihanouk Hospital Center of HOPE." This survey is conducted to fulfill two purposes: completion of my Master Degree and contribution to antiretroviral therapy program in Cambodia. The information you give to me is very important and therefore kindly be sincere in your responses. I assure you that the information that you provide to me will be handled with total confidence and nobody will identify your name. Your name will not be written on the questionnaire or kept in any other records. Your participation is voluntary and you can decide to stop the interview at any time.

Signature…………………………………..Date……………………………
………

Appendix 2: Questionnaire for interview

(A) Basic Information

Date of interview.   _____

Study site.   _____

Code of the interview ……………………………

WHO stage of respondent……………………..

(B) Socio-Demographic Information

1. Sex of participant: (1) Male [ ]   (2) Female [ ]

2. How old are you?...

3. What is your marital status?

    1). Single [ ]

    2) Married [ ]

    3). Separated   [ ]

    4) Divorced [ ]

    5) Widowed [ ]

    6) Widower [ ]

    7) Co-habiting (not married but living with partner) [ ]

4. Where do you live?

1) Phnom Penh [ ]

2) Province [ ]

(C) Socio-Economic Information

5. What is your education background?

1) Illiterate [ ]

2) Primary school [ ]

3) Secondary school [ ]

4) High school [ ]

5) University [ ]

6**.** What is your occupation?

1) Unemployed [ ]

2) Farmer [ ]

3) Civil servant [ ]

4) Small business/self-employed [ ]

5) Company worker [ ]

6) NGOs staff [ ]

7) Others (specify)………………………………..

7. How much money do you earn per day?

…………………………………………………………….

8. How much do you spend per day?

…………………………………………………………….

9. Do have enough food to eat every day?

　　　　　1) Yes [ ]

　　　　　2) No [ ]

(D) Knowledge of ART Drugs

10. Why do you take ARV drugs?

　　　1) To cure HIV/AIDS [ ]

　　　2) Not for curing HIV/AIDS but to prolong life [ ]

　　　3) Reducing pain [ ]

　　　4) Stop progression of HIV/AIDS [ ]

　　　5) I don't know [ ]

　　　6) Others ……………………………………………………………

11. How many ARV drugs need to be taken together for effective treatment?

　　　　　1) Do not know [ ]

　　　　　2) One ARV drug [ ]

3) Two ARV drugs [ ]

4) Three ARV drugs [ ]

5) Others [ ]

12. How long is the ARV treatment?

1) Do not know [ ]

2) One month [ ]

3) Two months [ ]

4) Six months [ ]

5) Lifelong [ ]

6) Others …………………………………………………………..

13. What are the side effects that may happen during ART?

1) Skin rash [ ]

2) Gastro intestinal problem (Vomiting and abdominal pain…) [ ]

3) Night mare [ ]

4) Liver toxicity (jaundice on eyes and skin) [ ]

5) Anemia [ ]

6) Lipodystrophy [ ]

7) Others …………………………………………………………

14. What will you do if side effects happen?

1) Stop taking ARV by myself [ ]

2) Buy drug from pharmacy to treat side effect [ ]

3) Call doctor for advice [ ]

4) Go to hospital for consulting with doctor [ ]

5) Do not know [ ]

6) Others ……………………………………………………..

15. What are the benefits of taking ARV regularly, correctly and continuously?

1) Suppression of HIV viral load in blood [ ]

2) Avoidance of resistance of HIV to ARV [ ]

3) Achievement of ART success [ ]

4) Do not know [ ]

5) Others (specify………………….)

(E)Treatment Regimen

16. Which ART drugs are you currently taking?

Abacavbir (ABC)	1)	Yes	2)	No
Didanosine (DDI)	1)	Yes	2)	No
Stavudine (D4T)	1)	Yes	2)	No
Lamivudine (3TC)	1)	Yes	2)	No
Efavirenz (EFZ)	1)	Yes	2)	No
Nevirapine (NVP)	1)	Yes	2)	No
Tenofovir (TDF)	1)	Yes	2)	No
Lopinavir/ritonavir (KALETRA)	1)	Yes	2)	No
Zidovudine (AZT)	1)	Yes	2)	No
Others (specify)	1)	Yes	2)	No

17. What other drugs (besides anti-retroviral) are you currently on (tick as

appropriate)

Tick Drug and How many times per day

Tick	Drug	How many times per day
1	Appetitive stimulants/vitamins	
2	Antibiotics (other than TB)	
3	Co-trimoxazole prophylaxis	
4	Fluconazole prophylaxis	
5	Fungal infection treatment	
6	Pain killers	
7	Sleeping pills	
8	TB drugs	
9	Others (specify………………………)	

18. Do you have difficulty taking ARVs while using drugs in question 17?

1)   Yes   [   ]

(why?...)

2)   No   [   ]

(why……………………………………………..)

 (F) ART Side Effects

19. Did you experience drug side effects? If your answer is No, please skip the

question 20 and 21, and then go on to question 22.

1) Yes [ ]

2) No [ ]

20. What are the side effects that you experienced?

       1) Skin rash [ ]

       2) Gastro intestinal problem (Vomiting and abdominal pain…) [ ]

       3) Night mare [ ]

       4) Liver toxicity (jaundice on eyes and skin) [ ]

       5) Anemia [ ]

       6) Lipodystrophy [ ]

       7) Others (specify……………………………………)

21. Did side effects cause you to stop taking the medicines?

       1) Yes [ ]

       2) No [ ]

(G) Characteristics of ART Adherence and Reasons Reported for Missing ART Doses

22. Did you take ARVs regularly and correctly? If your answer is Yes, please go on to question 23 and then finish interview ; if your answer is No, please skip question 23 and go on to question 24.

       1)   Yes [ ]

       2)   No [ ],

23. What are the factors that help you take ARVs regularly, continuously, and

correctly?.......................................

24. What causes you not to take your tablets?

1) Developed toxicity/ side effect [ ]

2) Forgot to take ART [ ]

3) Felt better [ ]

4) Too ill [ ]

5) Fear of stigma/disclosure [ ]

6) Stock was finished [ ]

7) Drunk with alcohol [ ]

8) Too many pills/ pill burden [ ]

9) Other

(specify)_____.

25. Many people find it hard to remember to take every single dose; in the last one month, how many doses have you missed?

Name of drug	Number of doses missed

Thank you for taking time to participate in this interview

Appendix 3: Recommendation letter from APU to Sihanouk Hospital Center of HOPE

APU

Mr. Kevin O´Brien,
Executive Director
Sihanouk Hospital Center of HOPE
P.O. Box 2318, Phnom Penh 3,
Cambodia
Tel (855-23) 882-484
Fax: (855-23) 882-485
E-mail: info@sihosp.org

Dear Mr. Kevin O´Brien,

Let me introduce Dr. HING Kim, one of our graduate students in Public Health Management at Ritsumeikan Asia Pacific University, Beppu, Oita, Japan, where I am an associate professor and a permanent faculty member. Hereby I would like to introduce and recommend him to you for any possible support that he might need to conduct his field study and research at the Sihanouk Hospital Center of HOPE in Phnom Penh, Cambodia.

Dr. HING must complete his Master thesis in order to fulfill the requirements for graduation from the Public Health Management program of our Graduate School at Ritsumeikan APU. I hope that you will understand and accept this request for the sake of scientific research and study.

Please do not hesitate to contact me in case there are any questions related to his survey and research.

Nader Ghotbi, MD, PhD

Graduate School (Public Health Management)
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E-mail : nader@apu.ac.jp

Appendix 4: Recommendation letter from APU to National Ethics Committee for Health Research of Cambodia

APU

Ritsumeikan Asia Pacific University

July 22, 2010

His Excellency Professor ENG Huot
Secretary of State of the Ministry of Health
President of the National Ethics Committee for Health Research
Phnom Penh, Cambodia

Let me introduce Dr. HING Kim, one of our graduate students in Public Health Management at Ritsumeikan Asia Pacific University, Beppu, Oita, Japan, where I am an associate professor and a permanent faculty member. Hereby I would like to introduce and recommend him to you for any possible support that he might need to conduct his field study and research at the Sihanouk Hospital Center of HOPE in Phnom Penh, Cambodia. His research plan has been examined by the Ethical Committee at APU and accepted.

Dr. HING must complete his Master thesis in order to fulfill the requirements for graduation from the Public Health Management program of our Graduate School at Ritsumeikan APU. I hope that you will understand and accept this request for the sake of scientific research and study.

Please do not hesitate to contact me in case there are any questions related to his survey and research.

Nader Ghotbi, MD, PhD

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Appendix 4: Recommendation letter from APU to National Ethics Committee for Health Research of Cambodia

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Appendix 5: Permission letter from Sihanouk Hospital Center of HOPE

REF # TS/ST 2173 SHCH

Dear Dr Hing Kim,

On behalf of Sihanouk Hospital Center of HOPE, I am very pleased to welcome you to conduct a research on our cohort under the title "Barriers to Antiretroviral Therapy Adherence at the Sihanouk Hospital Center of HOPE, Phnom Penh, Cambodia".

I hope your study finding will be able to provide us significant factors that we should focus on to help our patients achieving good adherence and getting the most benefit from ART in our setting.

I wish you good luck and success in your study.

Best regards,

Thai Sopheak, MD
Director of the Infectious Disease Department and Community Projects
Sihanouk Hospital Center of HOPE
Telephone: (855) 011 842 034 / 092 759 230
Street 134, Sangkat Veal Vong, Khan 7 Makara
Phnom Penh, Cambodia

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Tel: (855-23) 882 484, Fax: (855-23) 882 485, Email: info@sihosp.org, Web: www.sihosp.org

Appendix 6: Permission letter of National Ethics Committee for Health Research of Cambodia for conducting field research

Dr. Hing Kim

Project: Barriers to Antiretroviral Therapy Adherence at the Sihanouk Hospital Center of Hope, Phnom Penh, Cambodia.

Reference: August 13th, 2010 NECHR meeting minute

Dear Dr. Hing Kim,

I am pleased to notify you that your protocol entitled "Barriers to Antiretroviral Therapy Adherence at the Sihanouk Hospital Center of Hope, Phnom Penh, Cambodia." has been approved by National Ethic Committee for Health Research (NECHR) in the meeting on August 13th, 2010. This approval is valid for twelve months after the approval date.

The Principal Investigator of the project shall submit following document to the committee's secretariat at the National Institute of Public Health at #2 Kim Il Sung Blvd, Khan Tuol Kok, Phnom Penh. (Tel: 855-23-880345, Fax: 855-23-881949):

- Annual progress report
- Final scientific report
- Patient/participant feedback (if any)
- Analyzing serious adverse events report (if applicable)

The Principal Investigator should be aware that there might be site monitoring visits at any time from NECHR team during the project implementation and should provide full cooperation to the team.

Regards,

Chairman

H.E. Prof ENG HUOT

#2 Blvd KIM YL SUNG, Khan Toul Kork, Phnom Penh , Tel : (855-23) 880 345 , Mobile phone : (855-12) 280 790, (855-12) 842 442