# WHY DO HIV-NAÏVE PATIENTS IN PHAYAO, THAILAND DELAY INITIATING ANTIRETROVIRAL THERAPY (ART)?

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**ABSTRACT:** Early treatment extends life expectancy for people living with HIV/AIDS, but many of them delay treatment initiation. We describe the characteristics, HIV status, and reasons for delaying and starting antiretroviral treatment (ART) among patients with HIV who were treatment-naïve and enrolled in an intervention study at HIV Clinic of Phayao Hospital, Thailand. The 23 participants were 18-54 years of age. Median CD4 cell count was 55 /mm$^3$ (range 6-218 /mm$^3$) when starting ART. Eleven patients were HIV-infected patients, who returned to receive treatment, and 12 patients were newly diagnosed with HIV. Among these twelve, eight suspected they were HIV positive but delayed seeking a diagnosis. Common reasons patients gave for delaying ART were that they did not know they were eligible and they had no symptoms. The most common reason for initiating ART was to be healthy. Late diagnosis of HIV infection and insufficient HIV healthcare information were reasons for delaying ART initiation among HIV-naïve patients in Phayao. Free treatments and availability of health services and medications did not assure that HIV-naive patients would decide to start taking ART.

**Keywords:** Delayed treatment, Anti-retroviral treatment, HIV-naive, Thailand

## INTRODUCTION

HIV infection has become a global health problem. In 2012, the United Nation of AIDS reported there were 35.3 million people around the world living with HIV infection and 2.3 million were new of HIV infections [1]. In Thailand as of March 2011, the Bureau of Epidemiology Department of Disease Control reported that the Thailand prevalence rate of AIDS was 621.46 per 100,000 population and the AIDS case fatality rate was 26.32%. Since the beginning of the epidemic, Phayao has had 2.26 AIDS prevalence rate per 1,000 population, which was the highest prevalence rate of AIDS patients in the country [2].

To extend survival rates and improve the well being of people living with HIV/AIDS (PHA), antiretroviral treatments (ART) have been recommended globally. Thailand, a resource-limited country, has improved access to ART by promoting the National Access to ART for People Living with HIV/AIDS (NAPHA) project and the availability of GPO-VIR - the Thai brand name of generic fixed-dose combination of stavudine, lamivudine, and nevirapine. By March 2007, more than 80,000 HIV-infected patients in Thailand were receiving ART [3]. On April 1, 2007, the NAPHA project was transferred to the Thailand AIDS Foundation under administration of the Thailand National Health Security Office. The first Thailand National Treatment Guidelines specify that PHA are eligible for starting ART under the following conditions: 1) when CD4 cell count is lower than 200 cells/mm$^3$; and 2) CD4 count is below 250 cells/mm$^3$and the patient has symptoms or has clinically defined AIDS [4]. The Treatment Guidelines also cover CD4 cell investigation twice a year, viral load determination once a year, counselling services, and treatments and care for Thai PHA at no cost [5]. These Guidelines resulted in 112,931 Thai PHA receiving ART and 60,657 PHA receiving CD4 cell count investigations at least two times per year in 2008 [6].

However, preliminary evaluations of ART in

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Thailand showed that HIV treatment-naïve patients were more likely to initiate ART when their CD4 cell counts were, on the average, under 80 cells/$mm^3$ [7-11]. At the same time, others have reported that the CD4 count at the first HIV diagnosis was higher than 250 cells/$mm^3$ [8, 12]. Patients who delayed initiating ART were more likely to get opportunistic infections (OIs) and less likely to respond to ART [13], especially if they started ART with a CD4 count below 50 cells/$mm^3$. Rates of OIs in HIV patients in Thailand with CD4 < 50 cells/$mm^3$ were 4.4 times higher than those who had CD4 cell > 50 cells/$mm^3$ once ART was initiated [14]. Factors related to delayed entry to care include gender difference, psychological responses, lacking health insurance, drug abuse, and unemployment [12, 15, 16]. The main reasons for delaying entry into care among HIV non-disclosed patients were being healthy, and fear of being stigmatized [17]. In 2013, in scaling up ART, Thailand had launched the new treatment guideline that PHA were able to initiate treatment when their CD4 level is lower than 350 cell/$mm^3$ [18]. Little, however, is known about whether or not healthcare financial issues and availability of medication in Thailand are related to a delay in initiating ART, particularly, in Phayao Province, where there are no studies about delayed treatment among new patients with HIV. The purpose of this paper is to describe the characteristics of patients who were HIV treatment-naïve and the reasons they gave for deciding to receive ART.

## MATERIALS AND METHODS

### Research setting

The study was conducted at HIV outpatient clinics of Phayao Hospital. This setting is the biggest HIV clinic located in the province and provides care to > 1,000 patients infected with HIV. This province has one of the highest rates of HIV-infection and HIV mortality in the country. The HIV clinics provide HIV/AIDS care, including pre and post-test counselling, follow-up evaluations, ART, and group activities for people living with HIV infection. Ethical approval was obtained from Ethical Review Board for Research in Human Subject, Phayao Public Health Office.

### Participants

Inclusion criteria for this study were as follows: (1) the HIV-infected patients who attended an outpatient clinic to start ART with a CD4 count< 350 cell/mm3 or had no symptom of HIV; (2) adults aged > 18 years and had never received ART; (3) they were eligible to receive ART according to the National Treatment Guideline for HIV/AIDS; and (4) agreed to participate in the study. PHA who were designated by a physician to not be ready to start ART according to the National Treatment Guideline for HIV/AIDS were excluded from the study.

### Materials

Structured questionnaires were developed by the researcher to collect socio-demographic data and clinical characteristics including age, gender, marital status, educational level, occupation, years of HIV infection, CD4 counts at ART initiation, and stage of HIV infection, reasons for delaying treatment, and reasons for seeking treatment at the present time. The developed questionnaires were validated by three experts of HIV treatment and care.

### Data collection and analysis

Data on socio-economic data and reasons for delaying treatment and reasons for seeking treatment at the present time were analysed and reported using inferential statistics including frequency, percentage, mean, and Standard Deviation.

## RESULTS

There were 23 HIV treatment-naive patients were recruited to the study. Among these, 12 were newly diagnosed with HIV (to be called "new patients") and 11 were treatment-naive patients who were returning to care (returning patients). In the 12 new patients, there were equal numbers of male and female patients. Most were middle-aged adults with a median age of 47.5 years (mean 46.33 ± 5.38; range 53-54), currently married status (83.33%), primary school level of education (66.67%), and agricultural labourers (66.67%). A majority of the returning patients were female (63.64%). Most were young adults with a median age of 37 years (mean 36.91 ± 11.93; range 18-53) and unemployed (54.54%) (Table 1). As illustrated in Table 2, all of the 12 new patients reported that they had been diagnosed within the past year. Three of them knew that they were HIV-infected patients when they were tested during pre-operative procedures. Two had been diagnosed with AIDS, and seven had symptomatic HIV infection. In addition, 8 of 12 new patients suspected that they had been infected for more than a year. Among the returning patients, 5 described having been diagnosed with HIV infection for more than 5 years; 4 were diagnosed when receiving prenatal care and 1 injection drug user was diagnosed

**Table 1** Socio-demographic characteristics of the 23 participants

| Variables | New HIV patients (N=12)* (%) | | Returning HIV-naïve patients (N=11)*(%) | |
|---|---|---|---|---|
| **Age** (years) | | | | |
| 18 - 27 | 0 (00) | | 3 (27) | |
| 28 - 37 | 1 (08) | | 3 (27) | |
| 38 - 47 | 5 (42) | | 2 (18) | |
| 48 – 57 | 6 (50) | | 3 (27) | |
| Mean | | 46.33 | | 36.91 |
| SD | | 5.38 | | 11.93 |
| **Gender** | | | | |
| Male | 6 (50) | | 4 (36) | |
| Female | 6 (50) | | 7 (64) | |
| **Marital status** | | | | |
| Single | 0 (00) | | 2 (18) | |
| Currently married | 10 (83) | | 5 (45) | |
| Widowed/ divorced | 2 (17) | | 4 (36) | |
| **Educational level** | | | | |
| No education | 1 (08) | | 0 (00) | |
| Elementary level | 8 (67) | | 8 (73) | |
| High school level | 3 (25) | | 3 (27) | |
| **Occupation** | | | | |
| Unemployed | 4 (33) | | 6 (55) | |
| Agriculture | 8 (67) | | 0 (00) | |
| General labour | 0 (00) | | 5 (45) | |

**Table 2** HIV Clinical Characteristics of the Participants

| Clinical data | New HIV patients (N=12)* (%) | | Returning HIV-naïve patients (N=11)*(%) | |
|---|---|---|---|---|
| **Years after the 1st HIV diagnosis** | | | | |
| < 1 | 12 (100) | | 0 (00) | |
| 1-3 | 0 (00) | | 3 (27) | |
| 3-5 | 0 (00) | | 3 (27) | |
| > 5 | 0 (00) | | 5 (45) | |
| **CD4 counts at ART initiation (cells/mm$^3$)** | | | | |
| < 50 | 7 (58) | | 4 (36) | |
| 51-100 | 2 (17) | | 1 (09) | |
| 101-150 | 2 (17) | | 1 (09) | |
| 151-200 | 0 (00) | | 2 (18) | |
| > 200 | 1 (08) | | 3 (27) | |
| Mean | | 67.25 | | 112.55 |
| SD | | 62.18 | | 88.51 |
| **Stages of HIV infection according WHO case definitions of HIV 2007** | | | | |
| Stage 3 condition | 9 (75) | | 8 (73) | |
| Stage 4 condition | 3 (25) | | 3 (27) | |

earlier but refused treatment at the time of diagnosis. The groups differed on their CD4 counts. The median CD4 count of the new patients was 43.5 (mean 67.25 ± 62.18; range 9-208), while the median CD4 count of the returning patients was 149 (mean 112.55 ± 88.51; range 2-218). Approximately 75% of the participants in both groups had stage 3 HIV infection according to WHO case definitions of HIV 2007.

**Reasons for delaying initiating ART**

The participants described different reasons for delaying initiating ART (Table 3), although similar reasons were given by new and returning patients. Seventy five percent of new patients stated that they delayed ART initiation because they did not know the eligibility criteria to start taking ART, while 64% of returning patients reported they delayed initiating ART because they did not qualify

**Table 3** reasons for delaying initiating antiretroviral therapy

| Reasons | New HIV patients (N=12)* (%) | Returning HIV-naïve patients (N=11)*(%) |
|---|---|---|
| - Did not know when to start taking ART | 9 (75) | 6 (55) |
| - Had good health- no symptoms of AIDS | 7 (58) | 6 (55) |
| - Did not qualify | 0 (00) | 7 (64) |
| - Did not know they were HIV infected | 6 (50) | 0 (00) |
| - Did not have time to see a physician | 2 (17) | 3 (27) |
| - Were not ready to take ART | 2 (17) | 3 (27) |
| - Feared side effects | 1 (08) | 3 (27) |
| - Did not believe in effectiveness of ART | 1 (08) | 2 (18) |
| - Worried about HIV seropositive status | 2 (17) | 0 (00) |

*One participant can answer several reasons

**Table 4** reasons for initiating antiretroviral therapy

| Reasons | New HIV patients (N=12)* (%) | Returning HIV-naïve patients (N=11)*(%) |
|---|---|---|
| - Wanted to be healthy, wanted to live longer | 8 (67) | 7 (64) |
| - Observed other HIV-infected persons who had taken ART and had good health | 4 (33) | 7 (64) |
| - Had no choices, the last hope, take or do not take ("I will die") | 2 (17) | 4 (36) |
| - Recommendations from healthcare professionals | 3 (25) | 2 (18) |
| - Taking ART for others- their children, husband, parents | 1 (08) | 4 (36) |
| - Worried about body images | 3 (25) | 1 (09) |
| - ART provided at no cost | 0 (00) | 1 (09) |

*One participant can answer several reasons

for ART. Seven of the new patients and 6 of the returning patients stated that they avoided ART because they were healthy. Among the 13 patients, one injection drug user had < 200 CD4 cell/mm$^3$, but the patient rejected initiating ART because of a perception of being healthy. Seven of the returning patients come to the HIV clinics for CD4 cell assessments every 6 months, but their CD4 cell counts were not low enough to qualify to begin ART. According to 7 returning patients, their CD4 cell counts dropped rapidly within the previous 6 months. Six of the 12 new patients had not suspected that they were HIV-infected; 3 were diagnosed during pre-operative procedures; and 3 were first diagnosed as infected when they exhibited symptoms of AIDS. A total of five patients reported that they had no available time to see a physician and were not ready to take ART. Three new and two returning patients reported they were afraid of the side effects of ART and did not believe in the effectiveness of ART, whereas only 1 new patient expressed concern about these matters. Additionally, 2 new patients were concerned about HIV stigmatization, but no returning patients expressed the same concern.

**Reasons for initiating ART**

The main reasons given by patients for initiating ART are described in Table 4. Fifteen patients, 8 new and 7 returning patients explained that ART would extend their good health. Therefore, they decided to start ART because they had avoided health problems from HIV infection. Most stated that they want to live longer. Eleven patients in both groups reported that they decided to start ART because they had learned about ART by observing their loved ones who were taking ART and experiencing good health and a high quality of life. Four returning patients and 2 new patients selected ART as their last hope. Only three new and 2 returning patients acknowledged that they decided to start ART because of recommendations by their doctors and/or nurse. One new and four returning patients described their decision to start ART to satisfy their loved ones. Three new female patients and 1 returning patient wanted to start ART to improve their physical image. Only 1 of 11 returning patients stated that she came to receive ART because she knew that she was able to receive HIV treatment and care at no cost.

## DISCUSSIONS

This study reports results on delaying HIV diagnosis and ART similar to the results of previous studies in Thailand [3, 7-11]. Nevertheless, we found differences between the newly diagnosed HIV patients and the returning patients according to age, CD4 status and reasons for delaying and/or seeking treatment. The participants in this study were older than those in recent studies in Thailand and were already disclosed. They were more likely to be experiencing severely opportunistic infections such as tuberculosis and meningitis according to the WHO case definitions of HIV 2007 [19] with a CD4 cell count much below that required for ART initiation. This is in contrast to results of studies in developed countries where patients start ART at a higher CD4 count [20, 21]. Two of the participants in this study died from advanced AIDS within two weeks after starting ART. According to the national evaluation of ART in Thailand, the AIDS mortality rate in the first 3 months after starting ART was 3.1% [22]. This situation in Phayao province strongly supports the argument of the association between delaying treatment and death after starting ART [14, 23].

In general, the main reasons for delaying initiating ART were delayed diagnosis of HIV infection, lack of information on when the patients should start taking ART, and the delay to seek medical care. Newly HIV diagnosed patients just avoided HIV investigation, even though they perceived themselves to have been infected before the current HIV investigation. Patients delayed returning to care because they believed that they were not eligible to take ART, did not know the eligibility criteria to start ART, or believed that they were healthy. This latter reason is similar to that found in previous studies in Thailand [9, 17]. The participants in this study attended primary school of level of education and lived in rural villages without access to health care information. They understood that they should start ART when they are getting sick.

The reasons given for deciding to take ART were similar to those in the studies from other countries [15, 16, 20, 21]. All patients in this study came to the clinics because they were experiencing symptoms of HIV infection and AIDS. Most mentioned that they decided to take ART because they wanted to live longer and wanted to be healthy. There are similar findings in the U.S. where patients decide to take ART to improve their quality of life [24]. The second most frequent reason to seek care at the HIV clinics was that they found other HIV-infected persons who had taken ART had good health. This might be an advantage of living in a community where knowledge can be transferred by observations and informal conversation, as long as the information is correct [25]. Few patients in this study reported that they were recommended by a physician or nurse to start taking ART. This may reflect that health counselling and pre-treatment care needs rapid scale up. Some female patients preferred treatment because they worried about their physical image from advanced disease. They also preferred to start ART because they wanted to be healthy so that they could provide the best care of their children, parents, and husbands. Conversely, no male patients reported that they decided taking ART because of their loved ones. One study in Thailand reported that Thai women had more accessibility to care than men [26]. At a time when the Thailand National Health Security Office has been trying to promote universal coverage for HIV investigation, treatments, and care with no cost, however there was no participant in the current study reported that they would like to start ART because of the availability of the medication and care.

Disclosed HIV patients of Phayao who were treatment-naïve started initiating ART very late. Late diagnosis of HIV infection and insufficiency of HIV healthcare information were main reasons of delaying ART initiation among HIV treatment-naïve in Phayao. Free HIV treatments and health services did not assure that HIV-naive patients would decide to start ART when they were eligible. Starting ART early is commonly found in the industrialized countries [27], but it is critical challenge, particularly in developing countries [28] where numerous people lack education. The major findings of this study indicate that scaling up diagnosis and treatment in Thailand is a very complex challenge. Starting treatment at a higher CD4 count (i.e., 550 or higher), increasing the frequency of CD4 investigation, or providing free ART with reimbursement for indirect costs, may not be effective to decrease the number of HIV-infected patients who delay treatment as long as an early HIV diagnosis is threatening, because of the stigma and the population lacking knowledge and awareness of the advantages of early diagnosis and treatment.

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