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THE CURRENT SITUATION OF ARV TREATMENT ADHERENCE, RELATED FACTORS AND INTERVENTION EFFECTIVENESS AT SELECTED OUT PATIENT CLINICS IN HANOI

SUMMARY OF DOCTOR OF PHILOSOPHY THESIS IN PUBLIC HEALTH

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INTRODUCTION

1. Study rationales

Human immunodeficiency virus (HIV) and Acquired Immune Deficiency Syndrome (AIDS) are among the most important findings that have significant medical, social and psychological effects in the late twentieth century. From the first few cases in Los Angeles in 1981 in men who have sex with men, HIV / AIDS has quickly become an epidemic with negative impacts on a global scale and Vietnam is no exception. According to the statistics of the Department of HIV / AIDS Prevention and Control by the end of 2017, ARV treatment was implemented in all 63 provinces / cities, with 401 ARV outpatient clinics with about 124,000 patients treated with antiretroviral therapy (ARV)

Antiretroviral drugs for HIV / AIDS treatment are seen as an important step in significantly reducing HIV-related mortality and the introduction of ARV drugs that have transformed HIV / AIDS infection from a deadly disease to a chronic disease which can be controlled. The main goal of antiretroviral therapy is to achieve sustained viral suppression and maintain immune function, thereby reducing mortality as well as the burden of disease. To achieve this, adherence to treatment plays an important role. However, adherence to treatment is not easy and most patients face difficulties with adherence to treatment.

Drug resistance is another cause for concern as a result of non-compliance. Although it is difficult to accurately quantify the effects of noncompliance, antiretroviral treatment is identified as one of the major causes of major public health threats. Because of the risk of developing resistance, not only to individuals but also to society.

Factors realted to compliance and interventions to enhance adherence to ART are also diverse. Interventions to enhance treatment adherence should be implemented to ensure social, cultural appropriateness and practical circumstances at the sites of intervention.

The thesis "*The current situation of ARV treatment adherence, related factors and intervention effectiveness at selected out-patient clinics in Hanoi*" was conducted with the following objectives:

1. Describe the situation and factors related to ARV adherence to HIV / AIDS patients treated at selected outpatient clinics in Hanoi city in 2016.
2. Assess the effectiveness of some interventions to increase ARV treatment adherence in Hanoi in 2017

2. Contribution of the thesis

This thesis is an effort to systematically study the situation and selected factors related to ARV treatment adherence 03 out-patient clinics in Hanoi. It is the first study to use a multi-dimensional assessment tool to assess treatment adherence in Vietnam. The design of interventions is built based on effective interventional models in the world and based on the characteristics of outpatient clinics in Vietnam. Interventions through on-site counseling and periodic telephone support for high-risk groups have demonstrated effectiveness in strengthening patient adherence.

1. Situation of ARV treatment adherence and some related factors in HIV / AIDS patients being treated at some outpatient clinics in Hanoi in 2016.

- The proportion of patients adhering to high, medium and low levels of treatment was 66.2%; 23.8% and 10%, respectively. About half of patients reported receiving support from

family, parents, or spouses in treatment. 9% of patients had encountered ARV side effects in the last 3 months and 1.2% of patients had to temporarily stop ART due to side effects.

- Experiencing side effects of drugs (AOR = 0.58; 95% CI: 0.41 - 0.82) is a negative factor affecting patients' adherence to ARV treatment. Supportive factors for adherence to treatment include the support of friends (AOR = 2.56; 95% CI: 1.49 - 4.35); disclosure of HIV status to family and relatives (AOR = 3.7; 95% CI: 1.32 - 10.00), not drinking alcohol in the past 30 days (AOR = 3.62; 95% CI: 1 , 95 - 6,7); have social support from health workers (AOR = 2.51; 95% CI: 1.40 - 4.52) and trust that oral medications are effective in helping to control the disease (AOR = 1.92; 95% CI: 1.78 - 3.56).

2. Effectiveness of the study interventions to increase ARV compliance in some outpatient clinics in Hanoi in 2017:

- The proportion of patients adhering to high levels of treatment increased from 66.2% to 84.4%. The proportion of patients joining peer support groups, reporting having received the support of a spouse or partner with ARV treatment, having a stable job increased by 10.6%; 53.6% and 43.5% before the study to 17.4%; 63.9% and 54.2% after the study, respectively. The proportion of patients experiencing side effects of the drug, having to temporarily stop taking ARV because the side effects significantly decreased from 9.0% to 3.5% and from 1.2% to 0.65%, respectively.

3. Scientific and practical significance of the thesis

3.1. Scientific significance

The thesis uses community intervention research design with comparison before and after the intervention. Tools, data collection techniques, and accurate and reliable data analysis. With the collected data, the thesis has determined the ARV adherence rate and some factors related to ARV adherence in HIV / AIDS patients in the study area.

3.2. Practical significance

The study has assessed the status of ARV adherence, relevant factors to have appropriate preventive interventions in ARV patients at some outpatient clinics in Hanoi. The research interventions are feasible, practical, and applicable on a broader scale

4. The structure of the thesis

The main body of the thesis is presented with 129 pages (*excluding appendices, tables of contents, abbreviations*) and is divided into: Introduction 2 pages; Chapter 1 - Overview: 44 pages; Chapter 2 - Research methodology: 16 pages; Chapter 3 - Research results: 38 pages; Chapter 4: Discussion 24 pages; Conclusion: 02 pages; Recommendation: 01 page and list of research projects 01 page. The thesis includes 47 tables, 06 figures and 05 pictures. References include 122 documents (15 Vietnamese, 107 English). The appendix includes a flowchart of counseling for compliance at outpatient clinics, training documents that reminds patients about the process of disclosing HIV status to their partners, and pre- and post-intervention data collection forms.

CHAPTER I : OVERVIEW

1.1. Antiretroviral treatment and benefits of antiretroviral treatment (ARV)

March 19, 1987 was considered an important milestone when for the first time the US Food and Drug Administration (US FDA) officially approved Zidovudine (Azidothymidine, AZT, ZDV) for HIV / AIDS treatment. Since then, efforts in drug research

and development have allowed the introduction of many ARV drugs to be applied for treatment. US FDA statistics show that up to now, more than 40 ARV drugs have been licensed and there are dozens of other research and development studies on new ARVs in the world. Diversity of treatment mechanisms as well as the diversity of drugs in each subgroup is a good opportunity, allowing patients access to many different treatment alternatioves, it, on the other hand, also shows the complex nature of ARV treatment as well as difficulties with adherence.

In Vietnam, antiretroviral treatment for HIV / AIDS patients has been standardized in the Minister of Health's Guidelines for HIV / AIDS Management, Treatment and Care, and later on, it was updated in the HIV / AIDS Treatment and Care Guidelines, issued together with the Minister of Health's Decision No. 5418 / QD-BYT of December 1, 2017. ARV treatment has now been covered by Health Insurance since early 2019 because foreign aid sources have been cut, and strict control of treatment adherence is important to limit drug resistance, which will lead to the use of the 2nd line and 3rd line regimens with significantly higher costs

The benefit of ARV treatment is not debatable and has been demonstrated in many clinical trial studies as well as in routine practice. Antiretroviral therapy provides patients with the opportunity to maintain a low viral load in the blood and below the undetectable threshold (less than 200 copies / ml of blood), which has been confirmed to have a protective effect for patients' health and prevent HIV transmission to sexual partners. UNAID official reports indicate that "an undetectable level of HIV viral load means that HIV is no longer transmitted".

1.2. The definition, importance of adherence to treatment, the assessment and the factors that influence adherence to treatment

According to the WHO definition, adherence to treatment refers to "*a patient's behavior in following a physician's instructions regarding the use of the medication as well as on diet or lifestyle*". Measuring patient adherence is a big challenge because of the subjective and private nature of the patient's medication behavior. These challenges are compounded by the fact that compliance is not only affected by the behavior of the patient, but also by the health system, socioeconomic status, and related factors to drugs.

Adherence to antiretroviral therapy is a special concern due to concerns about HIV drug resistance. Although no studies have accurately quantified the extent of noncompliance, and for how long it will lead to drug resistance, there is a high consensus in all studies and findings stating that non-adherence to treatment creates the risk of drug resistance, and therefore it is necessary to identify patients who do not comply with treatment for timely support. Studies and reports show that ARV resistance in Vietnam is not a big problem up to now. However, this does not guarantee that ARV drug resistance will not become a problem in Vietnam in the future.

Adherence to antiretroviral therapy has also been confirmed in studies to be positively associated with achieving viral suppression, increasing patient survival, as well as with CD4 immune status. There have been many studies on antiretroviral treatment adherence, showing that adherence to antiretroviral therapy below 95% increases the risk of not achieving viral suppression status. A large-scale study of 2,821 adult HIV-infected

patients in India compared the prevalence of viral suppression among patients who were on 80% to 89% of adherence to 100% of adherence and patients who were on 90% to 99% of treatment compliance compared with 100% of treatment adherence showed that the proportion of patients who achieved viral suppression defined as HIV-1 RNA below 400 copies / ml increased significantly when treatment adherence rates increased.

Adherence to treatment increases the life expectancy of patients and vice versa, patients who do not comply with treatment will have shorter life expectancy. A study conducted in India of 239 patients found that 57% of patients were determined to comply with ART. The study recorded 104 patients died during 358.5 patients-year and therefore the author calculated the death rate was 29 per 100 patients-year (95% confidence interval (CI): 23.9–35.2) and median duration of life of the patient was 6.5 months (95% CI: 2.7 –10.9). Mortality was statistically significantly higher among patients who did not comply with ART (64.5, 95% CI: 50.5–82.4) than patients who were on adherence (15.4 95% CI: 11.3–21.0). The risk of dying in patients who do not comply with ARV is 04 times higher than patients who do not comply with ARV (Adjusted hazard ratio: 3.9; 95% CI: 2.6–6.0).

There are different ways to assess adherence to treatment and it can be basically divided into direct and indirect methods. Indirect methods such as counting leftover pills, interviewing patients, interviewing pharmacists dispensing drugs, using high-tech equipment to monitor drug use such as MEMS devices (Medications Event Monitoring System). Direct methods such as measuring drug concentration in blood or urine, direct monitoring of patient medication use... Each method has its advantages and disadvantages. The United States Agency for International Development (USAID) has supported the development of this multidimensional assessment tool and has assessed the consistency and reliability of scales in a number of scare-resourced countries and has shown the usefulness of this tool. This multi-dimensional combination assessment tool was used in this study to investigate the status of treatment adherence at some outpatient clinics in Hanoi.

The antiretroviral adherence rate is estimated in many studies around the world as well as in Vietnam. Studies around the world have shown that adherence rates vary widely between locations, and rates range from 37% to 90%. In Vietnam, the use of different assessment tools at different locations also gives very different results. A study by Tran Xuan Bach et al. conducted in 2013 used a VAS visual toolkit to evaluate the result of treatment compliance rate of 94.5%. A study by Phan Thi Thu Huong et al. in Hai Duong and Dien Bien province in 2016 reported lower treatment compliance (60.4% and 63.4%). A number of other domestic studies have shown that compliance with treatment ranges from 60% to 80%.

Factors related to treatment adherence have been reviewed and evaluated by many authors. According to Reiter and Ickovics, it is possible to divide the factors affecting adherence to antiretroviral therapy into 5 main groups: factors belonging to patients, groups of factors belonging to treatment regimens, groups of factors belonging to the medical condition, a group of factors belonging to the relationship between patients and health workers and a group of factors belonging to the treatment facility.

Factors belonging to patients related to ARV adherence include: age, gender, ethnicity, education level, income level, reading status, and disclosure of infection status to others. Patients who disclosed their status to others reported in numerous studies are a positive factor in adherence to treatment. Disclosing one's status to others does not require the patient to hide the treatment which interfere with adherence.

Factors associated with the treatment regimen that may be related to adherence to the treatment include: side effects of the drug, number of tablets in the regimen, complexity of the regimen (number of daily doses, how use with or without certain foods), specific antiretroviral drugs, discrete tablets or fixed dose regimens. The research results largely show that the side effects of the drug have a negative effect on patient adherence. Several international studies have demonstrated that the use of a single pill regimen improves patient satisfaction, adherence and maintenance of viral suppression better than the multi-pill ARV regimen. Patient has never been on ARV.

Factors related to ARV adherence can include co-infection such as malaria, diabetes, and hypertension. Compliance with antiretroviral therapy will be reduced if the patient has additional co-infections. Patients with immune reconstitution syndrome (IRIS) are reported to have lower adherence rates than patients without this syndrome (RR 1.7; 95% CI 1.2–2.2 ; P = 0.001). A study by Vu Cong Thao in 2010 evaluating the status and effectiveness of care and support activities for HIV / AIDS patients showed that hepatitis B co-infection (HBV) and or hepatitis C (HCV) were identified to have a strong correlation with patient dropout with ORs of 10.8 and 8.99, respectively.

Factors that relate to the relationship between the patient and the health care provider that may affect adherence to treatment are patient satisfaction in general, patient confidence in the clinic, and patient confidence in staff members. Factors belonging to the treatment facilities related to ARV adherence include transportation convenience, clean and friendly environment, reasonable schedule, confidential treatment room, the service is provided comprehensively.

1.3. Interventions to increase ARV adherence

According to the World Health Organization (WHO), interventions that increase ARV adherence can be classified into groups such as Cognitive Behavioral Interventions (CBT), Educational Interventions, Treatment Support Interventions, Interventions direct treatment supervision, Intervention of active drug reminders, System-building interventions, Counseling interventions, Nutrition support interventions, Passive use of device reminders, Financial support interventions, Substance abuse treatment intervention, Depression treatment intervention.

Different authors also have different ways of classifying interventions that increase adherence. In the review of this document, for the purpose of analysis and comparison, we use the classification of interventions to enhance adherence to treatment according to the latest paper by Steve Kanters 2016. Interventions strengthening adherence to this treatment includes the following groups:

- *Standard of Care (SOC):* Including counseling, care and treatment practices at health facilities including adherence counselling, routine medical examination and treatment activities.
- *Enhanced Standard of Care (eSOC):* Including standard care combined with additional patient support, including additional counseling related to treatment adherence advice such as incorporating educational content and patient encouragement.
- *Phone interventions:* Includes interventions on the phone to assist patients. The frequency of calls can be from every 2 weeks to every 2 months. In some newly treated patients, the frequency of calls may be more frequent in the early stages.

- *Messaging (SMS):* This includes texting to the patient's mobile phone or research cell phone; including one-way and two-way messages, short messages or long messages at different frequencies (daily, weekly…)

- *Training in behavioral skills or treatment adherence training:* Includes training for patients on how to comply with ART, including modular training and interventions, as well as interventions and training life skills, behaviors, knowledge and attitudes

- *Multimedia intervention:* use online materials or information transmission materials.

- *Cognitive behavioral therapy (CBT):* Includes interventions to change behaviors and perceptions, as well as interventions from counselors using patient-encouraging interviews.

- *Supporter:* including the use of an individual (selected by the clinic or a patient of his or her own choice) to support patient adherence, including peer support, home visits, drug administration, treatment support, direct treatment monitoring therapy and customized direct treatment monitoring therapy.

- *Financial support:* Including conditional and unconditional financial supports, cash or vouchers.

- *Reminder device:* Medication reminders include calendars, alarms, pagers, dosing boxes, and other devices for managing and treating diseases.

In fact, the application of measures to increase adherence to antiretroviral therapy may be a single measure or a combination of two or more at the same time. A literature review comparing the effectiveness of interventions to increase adherence to ARV by Steve Kanters gathered and compared the results of 85 studies with 16,271 patients on the Cochrane Library, Embase, and MEDLINE. Research results show that short text messaging (SMS) is superior to routine care and treatment when analyzing studies globally (odds ratio [OR] 1.48; 95% KTC [CrI] 1,00–2,16) and research in developing countries (1,49; 1,04–2,09). Interventions that incorporate many measures have been shown to be more effective than interventions using single measures. Considering the virus suppression status, only cognitive behavioral therapy (CBT) (1.46; 95% CI: 1.05–2.12) and supporter intervention (1, 28; 95% CI: 1.01–1.71) is higher than standard care and treatment.

Treatment adherence interventions for patients using mobile phones, calling at appropriate frequencies, in combination with adherents for adherence to treatment, have been shown to be most effective interventions with odds ratio of 6.74 (95% CI: 2.87-16.55) in the analysis of global studies. The results of this intervention in developing countries (LMIC network analysis) also showed similar results with the difference ratio of 6.59 (95% CI: 2.95 - 16.06). The most pronounced effect of a combination of adherence to treatment advisor and patient phone for patients suggests this application due to its high feasibility and ease of implementation in countries with limited resources like Vietnam.

1.4. Information on Outpatient clinics (OPC)

Updated statistics from the Administration of HIV / AIDS Prevention and Control show that at the beginning of 2018, there were 271 outpatient clinics nationwide to pay for ARV treatment-related services and drugs. As international aid sources are reducing and to achieve the 90-90-90 goal set by the United Nations (90% of people know their HIV status, 90% of people have been diagnosed with HIV infection is continually receiving ARV treatment and 90% of people on ART achieve low and stable viral load), Ministry of Health strategies clearly define the continuation of OPC clinics and adopt the payment mechanism through health insurance since 2018.

CHAPTER 2. STUDY SUBJECTS AND RESEARCH METHODS

2.1. Study subjects

- Male or female aged 18 years and over, diagnosed with HIV infection and being on ART at outpatient clinics in the survey program.
- Agree to join the research.

2.2. Location, time and research design

Research location:

The study was conducted at 03 outpatient clinics (OPCs) providing HIV care and treatment for patients in Hanoi including: OPC Hoang Mai District, OPC Ung Hoa District and OPC Ba Vi District.

Research duration:

Pre-intervention research activities were conducted in October 2016 to December 2016. Post-intervention activities were conducted from November 2017 to December 2017.

Research design

Self-control intervention research method, with comparison before and after the intervention. At the selected research facilities, the research team, along with staff working at outpatient clinics treating HIV / AIDS, randomly selected patients based on a sampling frame at the time of pre- and post-intervention surveys.

2.3. Sample size and sampling methods

2.3.1. Sample size

The sample size in the pre-intervention study was calculated using the formula to estimate a proportion for cross-sectional survey.

$$n = \frac{(z_{\alpha/2} + z_{\beta})^2 \, p(1-p)}{\varepsilon^2}$$

The sample size after the intervention was calculated using a two-proportion comparison formula, with Chi-Square, two-sided test.

$$n = \frac{\left[z_{1-\alpha/2}\sqrt{2\,\bar{p}(1-\bar{p})} + z_{1-\beta}\sqrt{p_1(1-p_1)+p_2(1-p_2)}\right]^2}{(p_1-p_2)^2}$$

n = Sample size; p_1 = Pre-intervention adherence rate (estimated at 70%).

p_2 = Post-intervention adherence rate (estimated at 85%); $\bar{p} = \frac{p_1 + p_2}{2}$

α = Type I error (0,05); β = Type II error (0,1)

It shows that 322 patients are needed for this study. An additional 10% is estimated for loss to follow-up, so the study expects to recruit about 350 patients for pre- and post-intervention surveys. In fact, the study interviewed 352 pre-intervention patients and 350 post-intervention patients.

2.3.2. Sampling method

The sampling frame was developed based on the list of patients enrolled in ARV outpatient clinics. Random sampling is carried out using a single, non-repeat random

sampling method. Random sampling was conducted for both pre-intervention and post-intervention studies.

2.4. Intervention activities

2.4.1. Intervention objectives

- Increase ARV adherence rates for HIV / AIDS patients on ART at outpatient clinics within the scope of the program.
- Based on the results of building and piloting interventions, drawing experience to complete the model and deploy the model to other outpatient clinics.

2.4.2. Study subjects, location and timing of interventions

- Intervention subjects: Health workers and HIV / AIDS patients taking ARV treatment at Hoang Mai District Outpatient Clinic, Ung Hoa District Outpatient Clinic and Ba Vi District Outpatient Clinic.
- Intervention time: from July 2017 to November 2017 (4 months)

2.4.3. Content and intervention activities of the model

Interventions based on international experience have shown that patient-supporter interventions, combined with telephone reminders, are highly effective in developing countries. The person supporting the patient was the OPC clinic staff. These staff are direct counselors as well as to assist in reminding patients of adherence to treatment over the phone. In order to ensure effective counseling and telephone support, refresher trainings have been provided to OPC staff. On the other hand, due to the high workload at OPC, the intervention was identified as targeting only those at high risk of non-compliance. Interventions included

- *Refresher training for counselors and health care workers on adherence to treatment based on input surveys*
- *Maintain regular review activities on ARV treatment adherence in HIV / AIDS patients being treated at each visit*
- *Counseling every 2 weeks over the phone, focus on the subjects at high risk of non-compliance on ARV.*

2.4.4. Indicators to evaluate the effectiveness of the intervention

Based on research objectives

2.5. Tools and methods for data collection

Questionnaire for direct interview and medical records at OPC

2.6. Data management and analysis

Data were entered on EXCEL and analyzed using Stata 13 software.

2.7. Measures to control bias in research

Training on survey methodology, practice of survey skills for field supervision and quality control of questionnaires, selection of experienced investigators in social research.

2.8. Research ethics

The study was reviewed and approved by the Ethics Council of the National Institute of Hygiene and Epidemiology (Decision # IRB-VN01057-21 / 2016).

CHAPTER 3. RESEARCH RESULTS

3.1. Characteristics of research subjects before and after the intervention

The study collected data from 352 pre-intervention and 350 post-intervention patients, which is in line with the initial expected number of 350 patients. Among the subjects selected for this study, some did not answer a few questions or lacked some data to collect, so the statistics presented in the results of this study will be less than 350 or 352 and will reflect the number of patients with answers to each question.

Surveys before and after the intervention showed that men accounted for a significant proportion (about 2/3) of the study subjects. The educational level of the study subjects was not significantly different in the pre-intervention survey compared with the post-intervention with approximately 10% of the study subjects with primary education, about 1 / 3 of the research subjects have secondary school education and more than 1/3 of the research subjects have the secondary school level. The study noted a very small percentage of illiterate research subjects and approximately 10% of the research subjects had university and postgraduate degrees in the pre- and post-survey.

The study subjects had an average age (standard deviation) of 37.0 (± 7.4), the average HIV infection time was 5.1 (± 2.8) years, the duration of ART was 4.5 (± 2.5) years and the time from the time of diagnosis of HIV infection to the time of ART initiation was 265.8 days with a large standard deviation (456.4 days). The data was also repeated in 2017, showing that the duration of HIV infection and the duration of ARV treatment is longer than about one year before the survey.

The statistics show that the weight in the last visit before the study was 53.7 (± 7.7) kg and the weight in the last visit after the study was 54.4 (± 8) kg. The difference in body weight of the study subjects was not statistically significant ($p > 0.05$). The study noted that the prevalence of hepatitis C was 26.4%, Hepatitis B was 9.1% while other infections were less common. About two-thirds of the patients did not have any opportunistic infections in the 2016 survey.

The majority of patients participating in the study before and after the intervention were those living in Hanoi (approximately 80%), earning less than 5 million VND / month (approximately 80%), living with their families or relatives (approximately 95%). About two-thirds of the patients are married, about 15% are single and 17% are divorced or widowed. This result is similar in both pre-intervention and post-intervention surveys

3.2. Situation of ARV treatment before and after intervention

3.2.1. ARV regimens at outpatient clinics

The regimens used at OPC clinics include: 1c regimen (NVP + 3TC + AZT), 1d (EFV + 3TC + AZT), 1e (NVP + 3TC + TDF), 1f (EFV + 3TC + TDF) and other regimen is the one that does not belong to one of the four regimens. The point to note in calculating the percentages in this table is that although there were 352 patients surveyed before the intervention and 350 patients surveyed after the intervention, a small number of patients could

not be accurately identified. the patient's current regimen due to lack of medical information or lack of an original medical record, these patients were excluded from the denominator

Table 3.1 ARV regimens used at research OPCs

ARV regimes	Pre- intervention 2016 (n=342)		Post- intervention 2017 (n=343)		P value
	n	%	n	%	
1c (NVP+3TC+AZT)	42	12,28	49	14,29	0,56
1d (EFV+3TC+ AZT)	20	5,85	20	5,83	0,99
1e (NVP+3TC+TDF)	21	6,14	5	1,46	0,001
1f (EFV+3TC+TDF)	230	67,25	268	78,13	<0,001
Other regimes	29	8,48	1	0,29	<0,001

1f treatment regimen (EFV + 3TC + TDF) is popularly used in outpatient clinics with approximately 67% in the pre-intervention study, at the time of intervention, the study noted a number of a significant number of patients switched to 1e treatment regimen to the other regimens, which mainly switched to 1f regimen. The percentage of patients using the 1f regimen at the time of the post-intervention survey was about 78%, a statistically significant increase compared to the time before the study ($p = 0.001$).

The number of times taking ARV during the day as well as the number of pill patients use in a day was compared between the pre-intervention survey in 2016 and after the intervention in 2017. The results show the rate of patients taking ARV once / day in 2016 was 72.1%, a significant increase of 82.1% in 2017 ($p = 0.002$). The use of fixed-dose combination pills also improved before and after the intervention from 69.3% in 2016 to 82.4% in 2017 ($p <0.001$).

The study found that about 3.7% of patients in the 2016 survey had a change of treatment regimen in the last 1 year and this percentage increased slightly to 8.3% in the 2017 post-intervention survey. This regimen change is presented in more detail in the research results section, which shows a higher trend of shifting to a first line regimen in 2017 compared to 2016. The proportion of patients experiencing the effects side effect of ARV in the 2016 pre-intervention survey was 9.0%, in which a small proportion of 1.2% of patients discontinued due to side effects of ARV

The 2016 pre-intervention study noted a significant proportion (approximately 95%) of patients had not been tested for viral load in the last 12 months and only 5% of patients had a viral load test in the last 12 months. The reason was due to some technical difficulties, so the viral load test has not been implemented in these outpatient clinics during 2015-2016. This test was only performed in special cases, or in patients who have moved from another place to the study OPC. Regarding the support received for ARV treatment, the 2016 pre-intervention survey showed that about 50% of patients received support from spouses and

also about 50% of patients received support from friends. Less than a half of patients (43.5%) have stable jobs and only about 10% of them join peer support groups.

3.3. Situation of ARV adherence at the time before the 2016 intervention

3.3.1. Assess adherence to treatment by interviewing patients

Part 1 of the multi-dimensional assessment toolkit consists of four qualitative questions used to ask patients about adherence. Patients who answer all 4 questions as "no" will be categorized as "high level adherence", patients with 1 answer "yes" will be categorized as "moderate adherent to level therapy" and two or more "yes" answers will be ranked as "low level adherence".

Survey results before the study showed that 88.5% had no difficulty remembering to take the drug, corresponding to 11.5% of patients still find it difficult to remember the need for medication, although the patient is still continue taking the medicine when feeling better (99.4%) and the patient did not quit when he felt more tired (98.8%). When asked about whether a medicine has been missed in the past 4 days, 7.7% of patients reported having forgotten at least one dose.

3.3.2. Assess treatment adherence with a visual scale (VAS) at the time prior to the intervention

On a visual scale (VAS 0-10 cm), patients interviewed prior to the intervention reported an average adherence rate of 9.3 with a standard deviation of 0.73. The proportion of patients with a VAS score of 9.5 or higher (patients classified as highly adherent to treatment) in the pre-intervention survey reached 78.8%.

3.3.3. Assess adherence to treatment by checking knowledge of ARV use at the time prior to intervention

Component 3 of the multidimensional assessment is a knowledge-based assessment. Patients were asked for information about the medication they were taking to check their knowledge about the usage, dosage, timing, and other precautions. Research shows that an approximate 14% of patients answered incorrectly about the name of the drug, the way it was taken, or the dose, the timing of the medication, as well as the precautions for use.

3.3.4. Assess adherence to treatment by counting the number of tablets in the period at the time before the intervention

Component 4 of the multidimensional assessment is the inventory of drugs used by the patient. If a patient does not bring a vial or bag to check for the remaining number of pills, effort should be made to ask how many doses are left until today, thus calculating the adherence rate. The pre-intervention survey noted a high proportion (98.8%) of patients who brought the empty vial/bag of medicine to research sites to show that they have used up, or said that they have used up the medicine but did not bring the vial or medicine bag with them.

3.3.5. Assess adherence to treatment by multidimensional assessment scale at the time before the intervention

The multi-dimensional assessment is the combined result of direct patient interviews; on a visual scale (Visual Analog Scale-VAS), knowledge of medication, and inventory of leftover medications. The results presented in Table 3.2 are based on the number of patients who responded adequately (349 patients) regarding treatment adherence questions among the surveyed patients (352 patients).

Table 3.2 Pre-intervention adherence to treatment by multi-dimensional assessment method.

Adherence to treatment based on multi-dimensional scale	Pre-intervention (N=349)		Confidence Interval 95% (CI 95%)
	n	Percent %	
High level	231	66,2	61,2-71,2
Moderate level	83	23,8	19,4-28,6
Low level	35	10,0	7,1-13,7

The pre-intervention study showed that the proportion of patients who were on ARV adherence treatment at a high level was 66.2% (95% CI: 61.2% - 71.2%), the proportion of patients who were on ARV treatment the median level was 23.8% (95% CI: 19.4% - 28.6%) and the proportion of patients adhering to ART at low level was 10.0% (95% CI: 7,1% - 13.7%).

3.4. Selected factors associated with adherence to treatment

Table 3.3 presents the demographic, sociological and pathological factors and the correlation with ARV adherence in the univariate logistic regression analysis model.

Table 3.3 Demographic, sociological and pathological factors and the correlation with ARV adherence in univariate logistic regression analysis models

Characteristics		B	OR = exp (B)	CI 95% of OR	P value
Age	≥ 35	0.05	1.05	0.95-1.19	0.25
	Under 35 (*)				
Education	≥Undergraduate	0.20	1.22	0.85-1.55	0.15
	< Undergraduate (*)				
Gender	Female	0.52	1.69	1.05- 2.75	0.04*
	Male (*)				
Monthly income	≥5 mils	1.08	2.95	0.57-16.7	0.12
	Under 5 mils (*)				
Distance to OPC	<10 km	0.08	1.08	0.98-1.22	0.24
	≥ 10 km (*)				
HIV clinical stage	1 or 2	0.59	1.80	0.95-2.89	0.09
	3 or 4				
ARV drugs	1st line	0.46	1.58	0.82-2.53	0.10
	2nd or 3rd line (*)				
Opportunistic infections	Yes	-0.29	0.75	0.55-1.45	0.18
	No (*)				
Current CD4 level	>500 copies/ml	0.02	1.02	0.95-1.20	0.16
	≤ 500 copies/ml (*)				
Working hours	Unstable	-0.54	0.58	0.46- 0.75	0.02*
	Stable (*)				
Friend supports	Yes	1.43	4.17	1.56 - 11.1	<0,01*
	No (*)				

HIV status disclosure	Disclosured	1.17	3.23	1.28-8.33	0.03*
	Non-disclosured(*)				
Drinking in the past 30 days	No	1.73	5.64	1.75-18.12	<0.01*
	Yes(*)				
Social support of healthcare staff	Yes	1.00	2.73	1.45-5.11	0.03*
	No(*)				
Trust on medication	Yes	0.49	1.64	1.18-2.27	0.04*
	No(*)				
Experienced drug side effects	Yes	-0.76	0.47	0.32-0.70	0.02*
	No (*)				

Note: (*) Control group

Univariate logistic regression shows that demographic and sociological factors such as age over 35, education level of university or higher and income of 5 million or more are not significantly related to ARV treatment adherence. Univariate analyzes also showed that patients with friends 'support adhered to treatment better than patients without friends' support (OR = 4.17; 95% CI: 1.56 - 11.11), female patients adhered to treatment better than male patients (OR = 1.69; 95% CI: 1.05-2.75). Similarly, patients who disclosed their HIV status to their family and relatives adhered to treatment better than patients who had not revealed their infection status to their family or relatives (OR = 3.23; 95% KTC: 1,28 -8,33). Non-drinking in the last 30 days (OR = 5.64; 95% CI: 1.75-18.12), with social support from health workers (OR = 2.73; 95% of CI 1.45-5.11), female (OR = 1.69; 95% CI: 1.05-2.75) and believe oral medications are effective in helping to control the disease (OR = 1.64; 95% CI: 1.18 - 2.27) are positive factors for better adherence to treatment. Factors related to the patient's condition and treatment such as unstable working hours have negative effects on adherence in univariate analysis (OR = 0.58; 95% CI: 0.46 - 0.75), in addition to having side effects of the drug is one of the negative factors affecting adherence to treatment with an odds ratio (OR) of 0 , 47 (95% CI: 0.32-0.70). While other factors such as: HIV clinical stage, ART regimen, with or without opportunistic infections, current CD4 levels> 500 copies / ml are not statistically relevant with adherence to ARV treatment with the corresponding odds ratio (OR) of 1.80 (95% CI: 0.95-2.89); 1.58 (95% CI: 0.82-2.53); 0.75 (95% CI: 0.55 - 1.45) and 1.02 (95% CI: 0.95-1.20)

Multivariate logistic regression was performed to investigate demographic, sociological and pathological factors and their correlation with antiretroviral therapy adherence, results are presented in Table 3.4.

Table 3.4 Selected demographic, sociological and pathological factors and the correlation with ARV adherence in multivariate logistic regression models

Characteristics		**AOR**	**CI 95%**	**P value**
Working hours	Unstable	0.67	0.42 - 1.35	0.41
	Stable(*)			
Gender	Female	0.74	0.38 - 1.43	0.38
	Male(*)			
Friend supports	Yes	2.56	1.49 – 4.35	0.04

	No (*)			
HIV status disclosure	Disclosured	3.7	1.32 - 10.00	0.03
	Non-disclosured(*)			
Drinking in the past 30 days	No	3.62	1.95-6.7	0.03
	Yes(*)			
Social support of healthcare staff	Yes	2.51	1.40-4.52	0.02
	No (*)			
Trust on medication	Yes	1.92	1.78-3.56	0.01
	No (*)			
Experienced drug side effects	Yes	0.58	0.41-0.82	0.01
	No (*)			

Note: (*) control group

Multivariate logistic regression analysis showed that experencing drug side effects in the last 3 months were factors that negatively affected treatment compliance with AOR = 0.58 (95% CI: 0.41-0, 82). Meanwhile, the positive supporting factors for adherence to treatment include: With the support of friends AOR = 2.56 (95% CI: 1.49 - 4.35); disclosure the status of infection for family, relatives AOR = 3.7 (95% CI: 1.32 - 10.00), non alcohol drinking in the last 30 days AOR = 3.62 (95% CI: 1.95 -6,7), with social support from health workers AOR = 2.51 (95% CI: 1.40-4.52) and trust that oral medications are effective with AOR = 1.92 (95% CI: 1.78-3.56). Female gender and erratic working hours are considered to be not statistically correlated with treatment compliance in multivariate analysis.

3.5. Assess the effectiveness of interventions according to the indicators

3.5.1. Adherence to treatment using a multidimensional assessment scale before and after the intervention

The multi-dimensional assessment is the combined result of direct patient interviews; on a visual scale (Visual Analog Scale-VAS), knowledge of medication, and inventory of leftover medications. The effectiveness of intervention based on the proportion of patients adhering to high, moderate and low treatment levels is presented in Table 3.5. A point to note is that the calculation of treatment adherence is based on the total number of patients who have a full response to treatment adherence questions, so the number of patients included in the actual calculation is smaller than the total number of patients surveyed (352 patients before the intervention and 350 patients after the intervention).

Table 3.5: ARV treatement adherence before and after the intervention by multidimensional evaluation

Treatment adherence level	**Percentage % (CI 95%)**	
	Pre-intervention (N=349)	**Post-intervention (N=334)**
High	66.2 (61.2-71.2)	84.4 (80.1-88.1)
Moderate	23.8 (19.4-28.6)	14.7 (11.1-18.9)
Low	10.0 (7.1-13.7)	0.90 (0.2-2.6)

The study results showed that the compliance rate of ARV with high level before intervention was 66.2% (95% CI: 61.2% -71.2%) increased statistically and clinically significance after intervention to 84.4% (95% CI: 80.1% -88.1%) (p <0.001). Similarly, the adherence rate of ARV treatment with moderate and low level before intervention was 23.8% (95% CI: 19.4% - 28.6%) and 10.0% (95% CI: 7.1% -13.7%) decreased significantly and clinically to 14.7 (95% CI: 11.1% -18.9%) and 0.9% (95% CI: 0.2% -2.6%) after intervention (p <0.001)

3.5.2. Adherence to treatment based on interviewing patients before and after intervention

Survey results before and after the intervention showed that although the proportion of patients who found it difficult to remember the use medication had decreased slightly from 11.5% before the study to 9% after the study, the rate remained high. A comparison of the proportion of patients who did not find it difficult to remember the use of drugs before and after the intervention showed that the change was not statistically significant compared to the time before the study. Similarly, based on the response rate to other questions used to interview patients in component 1 of the evaluation, the study noted a similar rate as before the intervention in terms of the disease rate such as patients continued taking the medicine when they felt better (97.7%) and the patients did not quit when they felt more tired (97.7%). When patients were asked whether they had missed a dose in the past 4 days, 6.6% of patients still reported having forgotten at least one dose in the post-intervention survey compared to 7.7% before the intervention.

3.5.3. Compliance with treatment by visual assessment (VAS) compared before and after the intervention

On a visual scale (VAS 0-10 cm), the patients interviewed after the intervention reported an average adherence rate of 9.6 with a standard deviation of 0.82. VAS is a second component in a multi-dimensional rating scale. The proportion of patients with a VAS score of 9.5 or higher (patients classified as highly adherent to treatment) in the post-intervention survey reached 92.2%, statistically higher than with the time before the intervention.

3.5.4. Compliance through antiretroviral knowledge testing before and after intervention

The study showed that 86.1% of patients correctly answered all knowledge test questions before intervention and this percentage increased significantly (97.7%) after the intervention. These questions include questions about the name of the drug, how to use it, or the dose, when and how to use it, and precautions for use.

3.5.5. Comply with treatment by counting the number of tablets before and after the intervention

In the post-intervention survey, the study continued to record an almost (99.7%) of patients who brought the empty vial (bag of medicine) to show that they had used up, or answered that they had used it. A point to note is that if the patient does not bring the vial or bag to the inventory of the remaining pills, the staff should try and attempt to ask how many doses are left until today, from which treatment adherence rate was calculated. Compared to the adherence to treatment by counting the remaining pills in the pre-intervention survey (98.8%), there was no statistically significant difference on this index before and after the intervention (p > 0.05).

3.5.6. Use first line ARV regimen after intervention compared with before intervention

Compared to the pre-intervention survey, the proportion of patients using first line regimens in the study has increased from 91.5% to 99.7%. Among the first line regimens, the main change is the use of 1f regimen (EFV + 3TC + TDF).

3.5.7. CD4 values in the most recent test, compared before and after the intervention

A slight increase in CD4 test value in the last test recorded after the intervention (2017), which was 474.9 ± 216.1 cells / ml blood compared to the time before the intervention (2016) 452.2 ± 203.2 cells / ml blood ($p > 0.05$).

3.5.8. Testing for viral load in recent 12 months, comparing before and after intervention

The results showed that 5.1% of patients were tested for viral load in the last 12 months in the 2016 survey and this percentage has increased to almost all the patients (96.8%) in post-intervention survey in 2017. Compared to 2016, an additional 91.7% of ARV patients were tested for viral load to monitor their health status.

3.5.9. Family and social support for patient, comparison before and after intervention

The percentage of patients participating in peer support groups increased from 10.6% before the study to 17.4% after the study, the change after intervention was positive and statistically significant ($p = 0.009$). In the pre-intervention survey, the study found that 53.6% of patients reported receiving spouse or partner support for ARV. The percentage of patients receiving ARV support from their spouses and relatives after intervention increased to 63.9% in 2017 and this change is statistically significant ($p = 0.006$). With the support of family and society, the percentage of patients with stable jobs also increased slightly from 43.5% (2016) to 54.2% (2017), a statistically significant change. ($p = 0.005$).

The study recorded about 12.5% of patients reported using Methadone or suboxone treatment services in 2016 and this percentage increased slightly to 15.5% in the 2017 post-intervention survey. About 7% reported receiving no support from health workers or very little support in the pre-intervention survey. In the post-intervention survey, all patients identified that they had the support of health workers for ARV treatment. The percentage of patients who reported receiving "much" and "very much" support from health workers was about 70% before the intervention, which increased to over 80% in the 2017 post-intervention survey.

3.5.10. Risk behaviors for non-adherence to antiretroviral therapy, before and after intervention

Research shows that only a small percentage of patients use addictive drugs both before and after the intervention (approximately 10%). The point to note is that because no tests have been performed, the patient's notification of narcotic use should not be interpreted with caution. The proportion of patients using alcohol (drinking three or more units of alcohol in any one day) in the pre-intervention and post-intervention survey was similar, at approximately 50% and this difference was not significant.

An unfavorable behavior for ARV treatment is hiding HIV infection, not disclosing the infection status to relatives. The results of the pre- and post-intervention surveys are presented in Table 3.6

Table 3.6 Disclosure of HIV status to relatives

Status	Frequency (%)		P value
	Pre-intervention 2016	Post-intervention 2017	
Non-disclosure of HIV status	54 (16,0)	20 (5,9)	p< 0,0001
Disclosure of HIV status	284 (84,0)	317 (94,1)	

The pre-intervention study showed that about 84% of HIV-infected patients disclosed their status to relatives. A similar survey repeated in 2017 showed that about 10% more patients disclosed their status to relatives (94%), this difference is statistically significant.

3.5.11. Experiencing side effects of ARV and stopping the drug due to side effects

The proportion of patients experiencing side effects of ARV in the 2016 pre-intervention survey was 9.0%, a statistically significant reduction to 3.5% after the 2017 intervention (p = 0.003). The study also found that the percentage of patients who had to stop ARV due to side effects after intervention also decreased by about half, from 1.2% before intervention to 0.65% after intervention, although the reduction This is not statistically significant (p> 0.05).

3.5.12. The patient's level of confidence in the effectiveness of ARV as well as the ability to take drugs as directed by the doctor

The patient's level of confidence in the ability to take the drug in accordance with the doctor's instructions and the effectiveness of ARV drugs was surveyed and rated on a scale of likert from 1 (totally not confident) to 7 (complete confidence) in which a higher score corresponds to a patient's higher confidence. Survey results show that about 78% of patients in the pre-intervention survey reported confidence in the correct use of drugs prescribed by a doctor at a very confident level (6 points) and completely confident. (7 points). This percentage in the post-intervention survey is about 85%. Similarly, about 10% of patients were either completely unconfident or very unconfident in their ability to follow the guide of a physician in the pre-intervention survey, and this percentage decreased to about 5%. in the post-intervention survey.

About 88% of patients in the pre-intervention survey reported confidence in the effectiveness of ARV at a confidence level (6 points) and total confidence (7 points). This percentage in the post-intervention survey is about 95%. Similarly, about 3% of patients had little confidence in the effectiveness of ARV in the pre-intervention survey and this decreased to about 2% in the post-intervention survey. Based on the average confidence level of the drug's effectiveness, these results show that the patient's average score (± SD) increased from 6.0 (± 0.6) points to 6.2 (± 0.4) points, although this difference is not statistically significant.

3.5.13. Satisfaction with the patient's physical and mental health on ARV

Patient's self-assessment of physical and mental health status after ARV treatment was surveyed and evaluated on a likert scale of 1 (completely dissatisfied) to 7 (completely satisfied). The higher the score, the higher the degree of agreement with the patient. The

survey results showed that about 70% of patients in the 2016 pre-intervention survey reported that ARVs improved their physical health in satisfaction (6 points) and complete satisfaction (7 points). This percentage in the 2017 post-intervention survey is about 94%. Similarly, about 90% of patients in the 2016 pre-intervention survey reported that ARVs improved their mental health at satisfaction levels (6 points) and total satisfaction (7 points). This percentage in the 2017 post-intervention survey is about 95%.

3.5.14. Satisfaction with the information about how to take medicine is provided by the clinic doctor

About 90% of patients in the 2016 pre-intervention survey reported satisfaction with information on how to use the drug at very satisfied levels (6 points) and completely satisfied (7 points). This percentage in the 2017 post-intervention survey is about 95%.

CHAPTER 4. DISCUSSION

4.1. Situation of ARV treatment

4.1.1. ARV regimens at outpatient clinics

First-line ARV regimens, namely 1f, a combination of three drugs (EFV + 3TC + TDF) are commonly used in OPC. The Ministry of Health has issued guidelines and has standardized ARV regimens across the country towards public health approaches. The Ministry of Health has also established standard protocols for all patients when starting ARV. At the same time, ARV drugs are coordinated and provided free of charge to all treatment facilities nationwide, so the use of ARV drugs is highly consistent, in accordance with the instructions of the Ministry of Health. First-line regimens are inexpensive with costs of only 1/4 to 1/8 of the second-line regimens, effective for most patients, easily accessible due to the supply of drugs, which explains the large number of patients using first-line regimens.

Our study shows that the proportion of patients maintaining first-line ARV regimens in the pre- and post-survey surveys is high. This is very important for countries with limited resources, including Vietnam. In Vietnam, most facilities have only available first line ARV drugs and no other alternative regimens. In addition, second line drugs are not available in the domestic market but must be purchased internationally or through foreign aid programs. Therefore, maximizing the patient's adherence to the first line regimen and minimizing the switch to 2nd line regimens is important in maintaining the success of the treatment program.

4.1.2. Testing for viral load during ARV treatment

The 2016 pre-intervention study noted a small percentage of 5% of patients tested for viral load in the past 12 months. The reason mentioned is due to some technical difficulties, so the viral load test has not been implemented in these outpatient clinics during 2015 - 2016. This test was only performed in special cases or patients who have moved from another place who have had test results from other places. By 2017, the research results showed a positive change with the majority of patients tested for viral load in the past 12 months.

4.1.3. Some risk behaviors of patients being treated with ARV.

The 2016 pre-intervention survey showed that only an estimated 10% of HIV / AIDS patients on ARV reported having used heroin, opiates or marijuana in the past 30 days. Only 10% of the study subjects reported using drugs in the past 1 month in this study may be an estimate error due to the fact that the data collection is only conducted through data. through the interview. People with HIV / AIDS may not want to disclose their drug use when asked.

In this study, no urine or blood tests were performed to assess a patient's use of addictive substances.

About half of patients reported using alcohol in the past 30 days in the pre-intervention survey. This is a noticeable situation due to the consequences of alcohol use in general on the patient's health, interaction, drug metabolism and adherence to treatment that have been warned in many studies. Nonetheless, a higher proportion of patients report using alcohol compared to drug use, suggesting that alcohol use is considered more acceptable to people with HIV / AIDS.

4.2. Current status of ARV adherence

4.2.1. Adherence to treatment according to multidimensional assessment scale before the intervention

This study recorded 66.2% of patients adhering to high-level treatment according to a combination of patient interviews, VAS assessment, knowledge of drug use, and inventory of excess drugs. Compliance rates by multidimensional assessement were significantly lower than those for single-dimensional assessments indicating that patients with a good knowledge of ARV use did not necessarily mean compliance is satisfied.

Research by Phan Thi Thu Huong et all. on 250 AIDS patients managed and treated at Hai Duong HIV / AIDS Prevention and Control Center in 2016 reported lower treatment compliance rates compared to our study (60.4% vs. 66.2%). The results of this study are similar to the results of other surveys conducted by Phan Thi Thu Huong et all in 3 outpatient clinics in Dien Bien, 63.4% in 2016. Compared with a cross-sectional study of 252 HIV / AIDS patients with ARV inpatient treatment and outpatient treatment at A Thai Nguyen Hospital outpatient clinic by Do Le Thuy in 2012, the compliance rate of treatment The ARV in our study is lower (66.2% compared to 81.3%). Different studies have been conducted on different research populations with different definitions of treatment adherence, so the interpretation of treatment adherence in each study needs to be cautious.

4.3. Factors influence adherence to antiretroviral therapy

In our study, there were 6 factors related to adherence in multivariate analysis including the support of friends, disclosure of the HIV status to family and relatives, not drinking alcohol in the past 30 days, social support of health workers, trusting that oral medications are effective in helping to control the disease and the drug side effects.

Having support of friends, disclosing the status of infection to families and relatives are factors that positively influence the patient's ARV adherence with AOR 2.56 (95% CI: 1 , 49 - 4.35) and 3.7 (95% CI: 1.32 - 10.00). Meanwhile, in the opposite direction, drug side effects are the factors that negatively affect the patient's ARV adherence with AOR of 0.58 (95% CI: 0.41-0, 82).

The results of this study are consistent with the results of several previously published studies showing that the support of friends has also been confirmed to have a positive effect on treatment adherence. Patients do not disclose their infection status to others, leading to the fact that they have to hide their medication and this will affect adherence. Failure to disclose the infection status to relatives may also result in patients not receiving the necessary support from them and thus negatively affecting better adherence to treatment. The results of this study are also consistent with the conclusion in a meta-analysis that not disclosing their infection status to others increases the risk of non-compliance (OR = 3.46; 95% CI 2.04 to 5.89; I2 = 66%).

The findings of this study on patients experiencing ARV side effects and alcohol use would adhere to poorer treatment consistent with the results of the majority of studies showing adverse drug side effects negatively influence on patient adherence.

4.4. The effectiveness of interventions to increase treatment adherence in OPC

4.4.1. Adhere to treatment on a combined rating scale

Results of multidimensional assessment are the results of direct interviews with patients; on a visual scale (Visual Analog Scale-VAS), knowledge of medication, and inventory of leftover medications. The study results showed that the compliance rate of ARV with high level before intervention was 66.2% (95% CI: 61.2% -71.2%) increased statistically after intervention to 84.4% (95% CI: 80.1% -88.1%) (p <0.001). Similarly, the adherence rate of ARV treatment with moderate and low level before intervention was 23.8% (95% CI: 19.4% -28.6%) and 10.0% (95% CI: 7.1% -13.7%) decreased significantly to 14.7 (95% CI: 11.1% -18.9%) and 0.9% (95% CI: 0, 2% -2.6%) after intervention (p <0.001). These study interventions increased 18.2% of patients who were on ARV treatment with high levels (95% CI: 11.9% - 24.5%).

Compared with the results of Steve Kanters on ARV adherence enhancement measures, this study once again confirms the effectiveness of the combined intervention to use patient's supporters and remind the patient over the phone. This intervention model is considered by Steve Kanters to be highly effective (OR = 6.59 95% CI: 2.96-16.06) compared to standard care and treatment and the findings of this study are consistent with the author's.

The 18.2% increase in the number of patients who adhered to high levels of treatment is an encouraging result considering that the intervention did not create too much work burden for the OPC counselors. It is important to note, however, that when interpreting this outcome, the increase in compliance may not be entirely the result of the intervention. Repeated interviewing of patients after the intervention using the same questionnaire may be one of the factors that can cause deviations in measuring results as patients may recall previous interview questions and the answer will therefore be more accurate.

The second point to note when the interpretation of an intervention's increase in compliance is that the post-intervention assessment of treatment adherence is made immediately after the intervention ends, so the effectiveness of the intervention in this study the short term effect. The long-term effectiveness of the intervention has not been determined, therefore it is unclear how long the effects of this intervention will last

4.4.2. Use first line ARV regimen after the intervention compared with before intervention

The study showed that the proportion of patients using first line ART in the study increased from 91.5% to 99.7% compared to the time before the intervention. The most significant increase was in the 1f regimen (EFV + 3TC + TDF), increasing from 67.3% before intervention to 78.1% after intervention. For countries with limited resources such as Vietnam, it is important to maintain first line ARV regimens because most outpatient clinics as well as hospitals are available only on first line ART and no other alternative regimens. In

addition, second line ARV drugs are not available in the domestic market but must be procured internationally or relied on foreign aid. Therefore, good adherence to first line regimens is important to minimize drug resistance and minimize the switch to second or third line regimens with significantly higher costs.

This pre- and post-intervention study was conducted in 2016 and 2017, when the supply of ARV drugs was adequate under the National Program. Maintaining ARV treatment for patients is important and over the past 10 years, most of the costs of HIV / AIDS treatment, including ARV drugs, have been free from international fundings. Starting in 2019, these costs will be converted to health insurance coverage. According to the orientation of the ministry of health, in order to maintain and increase the number of HIV-infected people to continue receiving ARV treatment, PLHIV must have health insurance. Difficulties in implementing health insurance for people living with HIV have been mentioned and, therefore, more than ever, patients on ART and health workers should raise awareness about the difficulties that may be encountered in continuing ARV treatment for patients in the near future.

4.4.3. CD4 values in the most recent test, compared before and after the intervention

Although the CD4 count is no longer used to make ARV treatment decisions for HIV-infected patients. Routine CD4 testing is important to assess the patient's immune status and maintaining CD4 during treatment is important for patients to avoid other opportunistic infections.

The pre-intervention and post-intervention studies showed that patients maintained CD4 at a reasonable level (average of 452.2 ± 203.2 cells / ml before intervention and 474.9 ± 216.1 cells cells / ml after intervention, median is 444 cells / ml before intervention and 445 cells / ml after intervention). Compared to the number of CD4 cells in healthy people, it usually ranges from 500 - 1500 cells / mm3, patients in the study were mostly between 350 and 500 cells / mm3, meaning that the immune system was slightly impaired. This shows that the clinical effectiveness of the ARV treatment program at outpatient clinics participating in the study is very clear. The slight increase is not statistically significant CD4 in the post-intervention survey compared to before intervention may be partly due to the small impact of adherence to treatment or because the sample size has not been calculated large enough to test for changes in CD4. This issue should be further explored in further studies.

4.4.4. Viral load testing in recent 12 months, comparing before and after intervention

Significant increase in the proportion of patients tested for viral load in the last 12 months from 5.1% before the 2016 study to 96.8% in the 2017 post-intervention survey noted in the study. However, this should not be considered effective by intervention. Establishments participating in the study reported logistical difficulties prior to 2016 for viral load testing that led to the majority of patients not being tested and this problem was resolved in 2017

4.4.5. Risk behaviors to antiretroviral therapy non-adherence, before and after intervention

The 2016 pre-intervention survey showed that about 10% of patients reported using heroin, marijuana or opiates in 30 days and this percentage increased to about 15% in the 2017 post-intervention survey. First of all it should be noted that the determination of the use status is not done by testing but by asking the patient so that the rate of 10% or 15% of patients reporting the use of opiate substances has may be underestimating the use of

addictive substances in an HIV-infected patient population. This is understandable because drug use is illegal and the patient may not want to admit this to the interviewer. The increase in the number of patients reporting opiate use after intervention does not necessarily reflect an increase in opioid use, which may reflect greater patient confidence for interviewers and patients who shared the truth about their risk behavior more openly.

Similarly, no alcohol use in the past 30 days was reported in 53.2% of patients in the pre-intervention survey and this percentage decreased, but did not statistically to 46.5% after the intervention. The use of alcohol during treatment is unhealthy as well as adherence to treatment and this is strongly recommended for patients. The slight increase in the proportion of patients who have used alcohol in the past 30 days after intervention does not mean that the proportion of patients who use alcohol has increased. On the contrary, this may reflect the patient's greater confidence in the interviewer and the patient has shared the truth about his risk behavior more openly.

Having not disclosed their HIV status to their spouses, relatives is considered one of the risks for non-compliance with treatment. HIV disclosure was in fact, a part of the intervention has been implemented for those who were at risk of non-compliance with treatment. Non- disclosure of their HIV status to their spouses and relatives has led to the fact that patients have to hide their status as well as their medication. The pre-intervention survey study showed that about 84% of HIV-infected patients revealed their status to relatives. A similar survey repeated in 2017 showed that about 10% more patients revealed their status to relatives (94%). Similar to the above, the disclosure of one's infection status to others is a result of the patient's self-report, so the interpretation of the results should be cautious.

4.4.6. Experiencing side effects of ARV and stopping the drug due to side effects

The study results showed that the rate of patients experiencing side effects of ARV in the 2016 pre-intervention survey was 9.0%, significantly reduced to 3.5% after the 2017 intervention ($p = 0.003$). The study also showed that the proportion of patients who had to stop ARV treatment due to side effects after intervention also decreased by about half, from 1.2% before intervention to 0.65% after intervention, although this reduction is not statistically significant ($p > 0.05$).

Like any other drug, ARV can cause side effects for patients such as nausea (zidovudine (ZDV), stavudine (d4T), didanosine (ddI); abacavir (ABC), tenofovir) (TDF), indinavir, saquinavir (SQV), lopinavir (LPV), ritonavir (RTV). To prevent this side effect, counselors have instructed patients to take medication with meals except indinavir and didanosine. Patients have been reminded to be able to handle the side effects themselves, such as paracetamol, when they experience headache (may be encountered in the treatment regimen with drugs such as: ZDV, lamivudine (3TC) ... and to see, consult a doctor when having more severe side effects. Reducing the incidence of side effects as well as stopping ARV treatment because of the side effects in this study are encouraging results. A note is that the study patients are outpatient, so the side effects of the drug if any, were reported by patients themselves may not be always accurate.

4.4.7. The patient's level of confidence in the effectiveness of ARV as well as the ability to take drugs as directed by the doctor

Trust and the effectiveness of ARV treatment are an important factor to help patients adhere to good treatment and this has been determined in the study of the Tran Xuan Bach on HIV / AIDS patients. This study noted that interventions increased the percentage of patients who trust the effectiveness of ARV treatment at very confident level (6 points) and completely confident (7 points) by 7% (from 88% before the intervention to 95% after intervention). Similarly, the survey results showed that about 78% of patients in the pre-intervention survey reported their confidence in using the right medication prescribed by a doctor at a very confident level (6 points) and total confidence (7 points) and this percentage increased to approximately 85% after the intervention.

Although the research members have been adequately trained to carry out the assessment, the consistency and reliability of the data collected. Interpretation of results based on this evaluation should be taken cautiously as these results are self-reported, and there may be certain uncontrollable bias.

CONCLUSION

1. Situation, factors related to ARV adherence in HIV / AIDS patients treated at selected outpatient clinics in Hanoi city in 2016

- ARV regimens in outpatient clinics are mainly first-line regimens (91.5% of patients use first-line regimens). The 1f regimen (EFV + 3TC + TDF) dominates.
- A significant proportion of patients adhere to suboptimal ARV treatment
- The proportion of patients who adhered to the high, medium and low levels of treatment was 66.2%; 23.8% and 10%, respectively.
- The support received for people on ARV treatment is still limited and needs to be improved
- The proportion of patients receiving support from spouses and partners is 53.6%; from the family, parents is 50.8% and join peer support groups is 10.6%.
- About 9% of patients experience side effects of ARV and 1.2% of patients have to temporarily stop ART due to side effects of the drug.
- The majority of patients (90%) have a CD4 count and a small percentage (5%) have had a viral load tested in the past 12 months. The average CD4 test index of patients is 452.2 ± 203.2 cells / ml blood, median is 444 cells / ml blood

Compliance-related factors were identified in the study.

- Experiencing drug side effects (AOR = 0.58; 95% CI: 0.41 - 0.82) is a negative factor affecting ARV adherence. Positive support factors for adherence to treatment include: Friends' support (AOR = 2.56; 95% CI: 1.49 - 4.35); diclosure of HIV status to family and relatives (AOR = 3.7; 95% CI: 1.32 - 10.00), not drinking alcohol in the last 30 days (AOR = 3.62; 95% CI: 1 , 95-6,7); social support of health workers (AOR = 2.51; 95% CI: 1.40-4.52) and trust in effective oral medications to control disease (AOR = 1.92 ; 95% CI: 1.78-3.56).

2. Effectiveness of interventions to increase adherence to ARV at selected outpatient clinics in Hanoi in 2017

The effectiveness of the research interventions to enhance adherence to antiretroviral therapy is as follows:

- The proportion of patients adhering to high levels of treatment increased significantly (from 66.2% to 84.4%).

- The proportion of patients using 1st line ARV remained high and increased slightly (from 91.5% to 99.7%). The increase is mainly in 1f regimen (EFV + 3TC + TDF).

- The majority of patients were tested for CD4 cells (90% before and 95% after the study). Significant increase in the proportion of patients tested for viral load in the last 12 months from 5.1% prior to the 2016 study to 96.8%

- The proportion of patients participating in peer support groups, supported by spouses or partners with ARV treatment, having a stable job increased from 10.6%; 53.6% and 43.5% before the study to 17.4%; 63.9% and 54.2% after the study, respectively.

- Increase the proportion of patients who reported using opioid substances from approximately 10% prior to the study to about 15%. Approximately 84% of HIV-infected patients revealed their HIV status to relatives and this increased by approximately 10% after the intervention.

- The proportion of patients experiencing side effects of the drug significantly reduced (from 9.0% to 3.5%). The proportion of patients who had to temporarily stop ARV treatment due to side effects after intervention also decreased from 1.2% before intervention to 0.65%.

RECOMMENDATIONS

Based on the research results of the two rounds of surveys 2016 and 2017 and the results achieved during the intervention, the research team made some recommendations on the content of the intervention program to strengthen adherence to treatment for HIV / AIDS patients as follows:

1.Conduct screening and quick interviews with ARV patients in outpatient clinics to identify patients at high risk of non-compliance based on factors related to ART treatment compliance, thereby providing counseling and support for this group of patients.

2. Expand the pilot implementation, evaluate the effectiveness of intensive counseling interventions and periodically remind patients the use drug with the telephone support for patients of high risk groups who do not comply with treatment at clinics in other areas to make the effectiveness assessment more comprehensive.

3. Strengthen training for adherence counsellors to focus on the issues of drug use, drug-drug interactions for ARVs that need to be noted during treatment, and the HIV status disclosure issues for relatives.

LIST OF PUBLISHED ARTICLES RELATED TO THE THESIS

1. Dao Duc Giang (2017), "Antiretroviral drug treatment adherence at selected out-patient clinics in Hanoi and its related factors ", *Journal of Preventive Medicine* XXVII (9), pg. 11.

2. Dao Duc Giang (2018), " Effectiveness of interventions to increase adherence to antiretroviral therapy at selected outpatient clinics in Hanoi", *Journal of Preventive Medicine* XXVIII (4), pg. 27.