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# Effect of non-adherence to ARV therapy on 3-year life of HIV/AIDS patients: a cohort retrospective study

Hendra Dhermawan Sitanggang[1]*, Tri Yunis Miko Wahyono[2], Ira Marti Ayu[3]
[1]Program Studi Ilmu Kesehatan Masyarakat, Universitas Jambi
[2]Departemen Epidemiologi, Fakultas Kesehatan Masyarakat, Universitas Indonesia
[3]Program Studi Kesehatan Masyarakat, Universitas Esa Unggul Jakarta, Indonesia
*Corresponding Email: (hendrasitanggang@unja.ac.id)

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***Abstract***

***Background:*** *Adherence to antiretroviral therapy has become a challenge due to a lifetime of therapy. Adherence to antiretroviral therapy is one determining factor in the success of treatment. This study aimed to determine the influence of medication non-adherence on the 3-year survival of patients with HIV/AIDS.*
***Method:*** *This study used a retrospective cohort design conducted at RSPI Prof. dr. Sulianti Saroso. The sample was all HIV/AIDS patients from 2010 to April 2012, totalling 82 patients per group. Data analysis used Cox regression.*
***Results:*** *Multivariate analysis with Cox regression showed the factors that affected the 3-year survival of patients with HIV/AIDS are non-adherence to ART after being controlled by initial CD4 count (aHR = 7.608; 95% CI: 1.664 to 34.790) and non-compliance appointments after controlled by opportunistic infection, age and initial CD4 count (aHR = 2.456; 95% CI: 0.802 to 7.518). Among patients' non-adherence to ART, non-compliance appointments affected the 3-year survival of patients with HIV/AIDS after controlled by initial CD4 count, sex, CPT, modes of HIV transmission, WHO clinical stage, opportunistic infection, and age (aHR = 4.517; 95%CI: 0.729 to 27.987).*
***Conclusion:*** *Patients who do not adhere to medication and do not adhere to their medication appointments show a higher risk of dying than those who adhere to HIV/AIDS. Non-adherence to taking medication in the first year can be used as a marker to monitor medication adherence and the patient's health condition in the future. Therefore, monitoring adherence to taking the medication regularly through ARV therapy surveillance activities is essential.*

***Keyword:*** *non-adherence to ART, appointment keeping, survival, HIV/AIDS, cohort study*

**Abstrak**

**Latar Belakang:** Kepatuhan terhadap terapi ARV merupakan tantangan mengingat terapi ini harus dijalani seumur hidup. Kepatuhan terhadap terapi ARV merupakan salah faktor yang menentukan keberhasilan pengobatan. Tujuan penelitian ini adalah untuk mengetahui pengaruh ketidakpatuhan berobat terhadap kesintasan 3 tahun pasien HIV/AIDS.
**Metode:** Penelitian ini menggunakan desain kohort retrospektif yang dilaksanakan di RSPI Prof. Dr. Sulianti Saroso. Sampel pada penelitian adalah seluruh pasien HIV/AIDS periode 2010 – April 2012, berjumlah 82 pasien per kelompok. Analisis data menggunakan regresi Cox.
**Hasil:** Hasil analisis multivariat dengan *regresi cox* menunjukkan bahwa kesintasan 3 tahun pasien HIV/AIDS dipengaruhi ketidakpatuhan minum obat, setelah dikontrol variabel CD4 awal (aHR = 7,608 ; 95%CI : 1,664-34,790) dan ketidakpatuhan janji ambil obat, setelah dikontrol variabel infeksi oportunistik, umur dan CD4 awal. (aHR = 2,456 ; 95%CI : 0,802-7,518). Pada pasien yang tidak patuh minum obat, ketidakpatuhan janji ambil obat berpengaruh terhadap kesintasan 3 tahun pasien HIV/AIDS, setelah dikontrol variabel CD4

awal, jenis kelamin, PPK, faktor risiko penularan, stadium klinis awal, infeksi oportunistik, dan umur (aHR = 4,517 ; 95%CI : 0,729-27,987).
**Kesimpulan:** Pasien yang tidak patuh terhadap pengobatan dan janji ambil obat menunjukkan risiko kematian yang lebih tinggi dibanding yang patuh. Ketidakpatuhan minum obat pada tahun pertama dapat dijadikan sebagai penanda untuk memantau kepatuhan minum obat dan kondisi kesehatan pasien di masa yang akan datang. Oleh karena itu, penting untuk memantau kepatuhan minum obat secara teratur melalui kegiatan surveilans terapi ARV.

**Kata Kunci:** ketidakpatuhan minum ARV, ketidakpatuhan janji ambil obat, HIV/AIDS, studi kohort

## INTRODUCTION

The decrease in mortality and morbidity was the impact of finding Antiretroviral Therapy (ART) for people living with HIV/AIDS (PLWHA) in order to improve their quality of life (1–3). he UNAIDS report until December 2021 demonstrated that globally 38.4 million people were living with HIV, there were 1.5 million new cases in 2021, and 28.7 million people with HIV had received ART (4). Data revealed that in Indonesia, until May 2021, 27% of people living with HIV have received ART (5).

Adherence to ART is a significant challenge worldwide because it is a lifetime therapy (6). Adherence to ART is one of the essential factors in the success of therapy which aims to ensure the virological and clinical response of PLWHA (7,8). To achieve optimal viral suppression, World Health Organization (WHO) recommended that adherence to ART is at least 95% of the number of prescribed drugs (9). Adherence to drug appointments is also an essential factor in the success of ART and is also one of the indicators used by WHO in early warning against ARV resistance (HIV Drug Resistance Early Warning Indicators). This compliance means the patient is obedient in taking the drug according to the prescribed schedule (10).

The proportion of non-adherence to ART globally ranges from 33%-88% (7,11); in India, it ranges from 14%-86 (12); and in Indonesia, it ranges from 23%-77% (13–15). Several studies have shown the effect of non-adherences to ART, both adherence to medication and medication appointments, on the risk of death of HIV/AIDS patients (12,16–21). Information regarding the effect of medication adherence on the survival of HIV/AIDS patients has not been widely studied in Indonesia. Compliance with treatment in HIV/AIDS patients is an essential factor. Therefore, it is necessary to conduct a study to determine the effect of non-adherence to ART, both non-adherences to taking medication and taking medication appointments, on the 3-year survival of HIV/AIDS patients.

## METHOD

A retrospective cohort design study with a dynamic cohort population was conducted at the Infectious Diseases Hospital (RSPI) Prof. dr. Sulianti Saroso, Jakarta, Indonesia, in May-June 2015. This study's population was all HIV/AIDS patients at RSPI from 2010-April 2012. HIV patients aged 15 years who had received ART for at least one year since the beginning of ART were included. In contrast, pregnant patients with incomplete medical records were excluded. The minimum sample size was 82 respondents per group, calculated by the sample size determination methods for the survival analysis formula (incidence rate studies).

This study used medical record data, ARV monitoring, ART (follow-up) pharmacy data, and treatment overview. The independent variables in this study were non-adherence to taking medication and non-adherence to take medication appointments. Non-adherence to medication in this study is the patient's non-compliance in taking ARV drugs according to the prescribed dose. It is assessed from the number of drugs that are

not taken/remaining based on the patient's report at the time of the visit (taking the drug) (10,22). Patients were categorized as obedient if their medication adherence was 95% of the drugs given or prescribed. The measurement of non-adherence was according to the number of months of compliance divided by the number of months of follow-up for three years or until the event occurs (1,9,22). This variable has two categories: compliant >88% and non-adherent 88% using Receiver Operating Characteristic - ROC (sensitivity 85.7% and specificity 57.3%).

The second independent variable was non-adherence to drug appointments assessed based on the schedule for taking ARV drugs according to the prescribed schedule (10). This variable was measured by adding all the days late for taking medication according to the specified time during the first year of ART (17). Furthermore, this variable was categorized into compliant 12 days late and non-adherent to taking medication >12 days late using ROC (sensitivity is 71.4% and specificity is 49.3%).

The outcome of this study was the time of death observed until April 2015. This death incident can occur in the hospital (caused by AIDS or other diseases approved by the hospital) and outside the hospital, after the patient returns home/out of the hospital (death information came from the statement of the patient's closest family contacted by the hospital). Sensors in this study were patients who remained alive during the observation period or lost to follow-up from observation until the study was completed (23).

Data analysis used univariate, bivariate, and multivariate. The Log-rank test (Mantel-Cox) was used in the bivariate analysis and continued with the multivariate analysis using Cox regression.

## RESULT

Table 1 demonstrates that 2.3% of patients who do not adhere to taking medication and 11.4% of the patient who does not adhere to their drug appointments experience events. The highest proportion of events group was in the <30 years of age (16.7%), male (9.6%), and high school education level (10.0%). In addition, many of the HIV patients in the event group had initial CD4 <200 cells/mm3 (9.3%), transmission through bisexuality (33.3%), and received Cotrimoxazole Prophylactic Treatment (CPT) 8.7% in early clinical stage III (10.9%). A large proportion in the event group had opportunistic infections. There is tuberculosis (12.1%), toxoplasmosis (11.1%), candidiasis (14.3%), Pneumocystis Carinii Pneumonia (PCP) (50.1%), hepatitis (16.7%) and diarrhea (18.2%).

**Table 1.** Baseline Characteristics of Sample

| No. | Variable | Category | Event | | Sensor | | Total | |
|---|---|---|---|---|---|---|---|---|
| | | | n | % | n | % | n | % |
| 1 | Non-adherence to medication | Adherence | 12 | 15.6 | 65 | 84.4 | 77 | 100 |
| | | Non adherence | 2 | 2.3 | 85 | 97.7 | 87 | 100 |
| 2. | Non-adherence to medication appointment | Adherence | 9 | 11.4 | 70 | 88.6 | 79 | 100 |
| | | Non adherence | 5 | 5.9 | 80 | 94.1 | 85 | 100 |
| 3 | Age | < 30 year | 11 | 16.7 | 50 | 83.3 | 66 | 100 |
| | | ≥ 30 year | 3 | 3.1 | 95 | 96.9 | 98 | 100 |
| 4 | Sex | Female | 3 | 6.1 | 46 | 93.9 | 49 | 100 |
| | | Male | 11 | 9.6 | 104 | 90.4 | 115 | 100 |
| 5 | Education | Elementary | 0 | 0 | 8 | 100 | 8 | 100 |
| | | School | 1 | 7.1 | 13 | 92.9 | 14 | 100 |
| | | Secondary School | | | | | | |
| | | Senior High School | 12 | 10 | 108 | 90 | 120 | 100 |
| | | University | 1 | 4.5 | 21 | 95.5 | 22 | 100 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| 6 | Baseline CD4 | ≥ 200 cell/mm$^3$ | 1 | 4.2 | 23 | 95.8 | 24 | 100 |
| | | < 200 cell/mm$^3$ | 13 | 9.3 | 127 | 90.7 | 140 | 100 |
| 7 | Transmission Risk Factor | Heterosexual | 5 | 5.5 | 86 | 94.5 | 91 | 100 |
| | | Homosexual | 1 | 10 | 9 | 90 | 10 | 100 |
| | | Bisexsual | 1 | 33.3 | 2 | 66.7 | 3 | 100 |
| | | IDU | 7 | 11.7 | 53 | 88.3 | 60 | 100 |
| 8 | CPT | Yes | 13 | 8.7 | 137 | 91.3 | 150 | 100 |
| | | No | 1 | 7.1 | 13 | 92.9 | 14 | 100 |
| 9 | Baseline clinical stage | Stage I | 0 | 0 | 1 | 100 | 1 | 100 |
| | | Stage II | 0 | 0 | 25 | 100 | 25 | 100 |
| | | Stage III | 11 | 10.9 | 90 | 89.1 | 101 | 100 |
| | | Stage IV | 3 | 8.1 | 34 | 91.9 | 37 | 100 |
| 10 | Tuberculosis | Yes | 11 | 12.1 | 80 | 87.9 | 91 | 100 |
| | | No | 3 | 4.1 | 70 | 95.9 | 73 | 100 |
| 11 | Toxoplasmosis | Yes | 3 | 11.1 | 24 | 88.9 | 27 | 100 |
| | | No | 11 | 8 | 126 | 92 | 137 | 100 |
| 12 | Candidiasis | Yes | 4 | 14.3 | 24 | 85.7 | 28 | 100 |
| | | No | 10 | 7.4 | 126 | 92.6 | 136 | 100 |
| 13 | PCP | Yes | 2 | 50 | 2 | 50 | 4 | 100 |
| | | No | 12 | 7.5 | 148 | 92.5 | 160 | 100 |
| 14 | Hepatitis status | Yes | 1 | 16.7 | 5 | 83.3 | 6 | 100 |
| | | No | 13 | 8.2 | 145 | 91.8 | 158 | 100 |
| 15 | Diarrhea | Yes | 2 | 18.2 | 9 | 82.8 | 11 | 100 |
| | | No | 12 | 7.8 | 141 | 92.2 | 153 | 100 |

Table 2 states that the 3-year survival probability of compliant and nonadherent patients is significantly different (HR = 7.62 (95% CI: 1.71-34.05). HIV/AIDS patients with non-adherence were 7.62 times more likely to die than patients with adherence. In contrast, the 3-year survival probability of adherent and non-adherence patients based on non-adherence to medication appointments was not significantly different (HR = 1.98 (95% CI: 0.66 to 5.91). HIV/AIDS patients with nonadherent appointments had a higher risk of dying than adherence to appointments.

**Table 2.** Hazard Ratio of Non-adherence to ART, Non-compliance Appointments, and Covariate Variable to 3 years Survival HIV/AIDS Patients

| Variabel | Kategori | Probabilitas Kumulatif | Mean (bulan) | *Log Rank Test* | HR (95%CI) |
|---|---|---|---|---|---|
| Non-adherence to medication | Adherence | 0.831 | 33.99 | 0.001 | 7.62 (1.71-34.05) |
| | Non adherence | 0.976 | 35.78 | | |
| Non-adherence to medication appointment | Adherence | 0.881 | 34.32 | 0.183 | 1.98 (0.66-5.91) |
| | Non adherence | 0.938 | 35.47 | | |
| Age | ≥ 30 year | 0.968 | 35.65 | 0.002* | 0.16 (0.04-0.59) |
| | < 30 year | 0.822 | 33.93 | | |
| Sex | Male | 0.90 | 34.6 | 0.45 | 1.56 (0.43-5.61) |
| | Female | 0.935 | 35.5 | | |
| Tingkat Pendidikan | ≤ Junior High School | 0.952 | 35.08 | 0.480 | 0.48 (0.06-3.68) |
| | > Junior High School | 0.903 | 34.88 | | |
| Baseline CD4 | < 200 cell/mm$^3$ | 0.903 | 34.77 | 0.432 | 2.07 (0.27-15.85) |
| | ≥ 200 cell/mm$^3$ | 0.952 | 35.75 | | |
| Transmission Risk Factor | IDU | 0.872 | 34.25 | 0.196 | 1.92 (0.67-5.46) |
| | Non-IDU | 0.931 | 35.27 | | |
| CPT | No | 0.917 | 34.39 | 0.941 | 0.91 |

| | | | | | |
|---|---|---|---|---|---|
| | Yes | 0.909 | 34.95 | | (0.12-6.94) |
| Stadium Klinis Awal | Stage IV | 0.915 | 34.88 | 0.946 | 0.93 |
| | Stage I, II & III | 0.909 | 34.98 | | (0.31-2.78) |
| Opportunistic Infection (OI) | Severe | 0.885 | 34.53 | 01.12 | 3.07 |
| | Mild dan No OI | 0.961 | 35.7 | | (0.68-13.72) |

**P values ≤ 0.05 were considered as statistically significant*

A multivariate analysis was performed with the Cox regression. It was to determine the effect of non-adherence to taking medication and taking medication appointments on survival after controlling for the covariate variables. Prior did the multivariate analysis, the proportional hazard assumption tests all variables. The result is that all variables meet the assumptions.

Table 3 demonstrates the final model formulation (fit) based on the results of the multivariate analysis of the final model (fit) with the following formula:

H (t) = h0 (t) expβ1X1 + β2X2 + ……. +βpXp

Then get:

$$Y = h0(t)\exp\left[2.054\ (\text{non} - \text{adherence}) + 0.183(\text{CD4})\right]$$

Table 4 summarizes the final model formulation (fit) based on the results of the multivariate analysis as follows:

$$Y = h0(t)\exp[0.899\ (\text{non} - \text{adherence}) + 1.606\ (\text{IO})] - 2.173(age) + 0.902(\text{baseline CD4})]$$

**Table 3**. The Final Model of The Effect Of Non-Adherence to Medication On 3-Year Survival Of HIV/AIDS Patients

| Variable | B | SE | P-value | HR | 95% CI for Exp (B) | |
|---|---|---|---|---|---|---|
| Non-adherence to Medication | 2.029 | 0.776 | 0.009 | 7.608 | 1.664 | 34.790 |
| Baseline CD4 | 0.183 | 1.054 | 0.862 | 1.201 | 0.152 | 9.470 |

**Table 4.** Final Model of The Effect of Non-adherence Medication Appointment on Survival of Patients with 3 Years of HIV/AIDS

| Variable | B | SE | P-value | HR | 95% CI for Exp (B) | |
|---|---|---|---|---|---|---|
| Non-adherence to medication appointment | 0.899 | 0.571 | 0.115 | 2.456 | 0.802 | 7.518 |
| Opportunistic infection | 1.606 | 0.782 | 0.040 | 4.983 | 1.075 | 23.089 |
| Age | -2.173 | 0.782 | 0.001 | 0.114 | 0.031 | 0.419 |
| Baseline CD4 | 0.902 | 1.059 | 0.394 | 2.464 | 0.309 | 19.632 |

**Table 5.** The Association Non-Adherence to Medicine Appointment with Non-Adherence to Medication

| Non-adherence to medication appointment | Non-adherence to medication | | | | *p* | PR (95%CI) |
|---|---|---|---|---|---|---|
| | Non adherence | | Adherence | | | |
| | n | % | n | % | | |
| Non adherence | 51 | 64.6 | 28 | 35.4 | 0.001 | 2.11 (1.31-3.38) |
| Adherence | 26 | 30.6 | 59 | 69.4 | | |

HIV patients with non-adherent appointments are a higher proportion (64.6%) of nonadherence to taking medicine. In contrast, HIV patients with adherent appointments had a higher proportion (69.4%) of adherence to taking medication. We found that HIV/AIDS patients who did not adhere to appointments taking drugs in the

first year of ART were 2.11 times significantly more likely to be nonadherence to taking medication during follow-up compared to patients who adhered to medication (Prevalence Ratio=2.11 (95% CI: 1.31 to 3.38). The result is shown in Table 5.

## DISCUSSION

The results showed that non-adherence to ARV therapy affected the 3-year survival of HIV/AIDS patients. It is similar to previous studies in India that patients who are not compliant with ARV therapy have a 3.9 times risk of death compared to compliant patients (aHR = 3.9; 95%CI: 2.6 to 6.0). It has been controlled by age, sex, education, income, CD4, IO, distance to the place of ARV collection, and referral sources (12). In this study, the compliance assessment was based on pill count, with the category of adherence >95%.

A previous study in Southwestern Ethiopia reported that HIV/AIDS patients who did not adhere (low) to ART had a 3.78 times higher risk of death than patients who adhered (high) (aHR value = 3.78 (95%CI: 1.77 to 8.46). It has been controlled by sex, age, initial body weight, initial CD4 cell, TB infection, opportunistic infection, and clinical stage (24). Compliance assessment is based on the number of pills during the treatment visit, where 95% is said to be compliant (high) (1,25). *Compliance* can also be defined as the act or quality of sticking to something to obey something. Therefore, adherence to treatment means a more collaborative process between patient and provider. Patients have an active role in the care and commit to following the prescribed regimen as best as possible (26).

Antiretroviral (ARV) cannot eliminate HIV but control the virus replication. Viral replication can be suppressed if ARVs are taken regularly and continuously (6,27). WHO recommended monitoring and evaluating adherence regularly at each visit. It means that achieving good virological suppression requires high adherence to ART. The patient's non-adherence to taking ARVs can lead to the failure of ART. Cooperation, communication and a good treatment atmosphere will help patients comply with ART (1,25). Non-adherence to taking medication can increase the possibility of HIV mutating due to failure to suppress viral replication, thereby allowing drug resistance and an increased risk of death. Moreover, if they do not comply with ART, the destruction of the cellular immune system will fail to be prevented. The impact is decreased CD4 cells, the possibility of opportunistic infections, and an increased risk of death (16,28).

Non-compliance with drug appointments also affected our study's 3-year survival of HIV/AIDS patients. The results of multivariate analysis showed that HIV/AIDS patients who did not adhere to medication had a 2.5 times higher risk of death than an adherent patient after controlling for opportunistic infection variables, age, and initial CD4 cell count (aHR= 2,456; 95%CI: 0.802 to 7.518). However, it is not statistically significant when viewed from the confidence interval (CI) value which exceeds the value of 1. The CI range that passes the value of 1 is assumed to have a small sample size. If the sample is enlarged, it is assumed that the CI range will be above the value of 1.

Adherence to drug appointments was assessed only for the first year of ART. It is assumed to describe adherence to the next appointment to take the drug. This adherence measurement is the same as the study by Park et al. (2006) in South Korea, where the measurement of adherence used is the number of days late for one year with the same inclusion criteria, namely HIV/AIDS patients who have received ART for one year. The study's results are also consistent with this study; namely, the number of days late affects the survival of HIV/AIDS patients after controlling for clinical category based on the CDC and the number of new drugs at the time of starting ARVs (17). One previous study in Birmingham also reported that HIV/AIDS patients who did not adhere to their drug appointments in the first year of ARV therapy had a 2.9 times higher risk of death compared to adherent patients (aHR=2.9; 95%CI: 2.38

to 6.56) after controlling for age and baseline CD4 (20).

If the patient is non-adherent to taking medication in the first year, it indicates that he or she is not compliant with future medication appointments and has a risk of non-adherence (PR = 2.11; 95%CI: 1.31 to 3.38). It can lead to an increased risk of drug resistance and death in PLWHA, so monitoring adherence to drug appointments is crucial. Non-adherence to taking this medication can be used as an indicator or marker to identify or monitor HIV/AIDS patients at risk of developing poor health conditions in the future (17,20).

Based on the results of multivariate analysis, age was a confounder variable in the relationship between non-adherence to drug appointments and the 3-year survival of HIV/AIDS patients. Age ≥30 years as a protective factor with HR = 0.124 (95%CI: 0.034 to 0.449) on the effect of non-adherence to taking medication and HR = 0.054 (95%CI: 0.008 to 0.350) on the effect of non-adherence to taking medication. It could be related to irregular lifestyles in the age <30 years (as teenagers and young adults)—peers much influences this lifestyle. It can also affect their adherence to ART, including taking drugs. This condition makes them more at risk of death.

The opportunistic infection is also a confounder variable on non-adherence to drug appointments (HR = 5.394; 95%CI: 1.181 to 24.638) and the effect of non-adherence to taking medicine on 3-year survival HIV/AIDS patients (HR = 12.607; 95%CI: 1.362 to 116.72). HIV/AIDS patients with severe opportunistic infections risk 5 or 12 times more rapidly dying than those without mild opportunistic infections. In this study, severe opportunistic infections included tuberculosis, toxoplasmosis, PCP, hepatitis B and C, while mild opportunistic infections included diarrhea and candidiasis.

The emergence of opportunistic infections can decrease HIV/AIDS patients' immunity. It also becomes a clinical-stage marker in HIV/AIDS patients. The worse the opportunistic infection suffered, the higher the clinical stage. The worsening clinical condition also increases the risk of death. The presence of opportunistic infections, especially severe opportunistic infections, will increase the number of drugs, affecting adherence to medication for HIV/AIDS patients, including medication adherence.

The study at Arifin Achmad Hospital Pekanbaru revealed that the incidence rate of opportunistic infections (TB, lung pneumonia, lung abscess, and meningitis) was 0.029/100 person-time. It also found HIV/AIDS patients with mild opportunistic infections (skin disease, common pneumonia, herpes) of 0.021/100 person-time (29). This study is also linear with previous research at the RSPI-SS Jakarta. It reported that tuberculosis affected the 3-year survival of HIV patients receiving ARV therapy. HIV patients with tuberculosis have a 1.6 times higher risk of death than patients without tuberculosis (HR=1.6; 95%CI: 0.958 to 2.672) (30).

In this study, baseline CD4 affects the survival of HIV/AIDS patients, with HR = 1.201 (95%CI: 0.152 to 9.470) on the relationship between non-adherence to taking medication with patient survival and HR = 2.464 (95%CI: 0.309 to 19.632) on the relationship of non-adherence to medication appointment. It means HIV/AIDS patients with initial CD4 <200 cells/mm3 have a 1.2 times or 2.5 times higher risk of death than patients with baseline CD4 of 200 cells/$mm^3$. It is in line with the study at the RSPI-SS, which showed that the initial CD4 affected the survival of 3-year HIV/AIDS patients, with HR = 2.06 (95% CI: 0.489 to 8.687) (30).

HIV infection attacks T-helpers and macrophages with CD4 receptors in the body, where these cells play an essential role in the human immune system. Several CD4 lymphocytes will be destroyed and decrease the CD4 count. Low CD4 cells indicate a decrease in the body's resistance or impaired immunity, which can increase the risk of opportunistic infections and ultimately increase the risk of death. The emergence of opportunistic infections will also cause an increase in the number of HIV/ AIDS taking drugs. Consequently, it will affect their adherence to ART (31).

## LIMITATION OF THE STUDY

Information bias on the medication adherence variable might be there since the information obtained from the patient's acknowledgement (self-reported) of the number of pills left or not taken. Several factors make the patient not report as they should. They do not want to be reminded by health workers to be considered amenable, or patients fail to remember the number of pills they have not taken (how many times they have not taken their medicine). This information bias existed in both groups (adherent and non-adherent)-called a non-differential bias.

The death status in this study is death caused by HIV/AIDS or other diseases confirmed by the hospital. It was difficult to obtain information on the causes of death of HIV/AIDS patients, so the researchers assumed that all deaths were due to HIV/AIDS. We get the death information from medical records, telephone contacts, and drug-taking supervisors. However, some patients lost follow-up- 4 patients (8.5%) stopped the therapy, and five (3%) were referred to other health services. As a consequence, the death status was unknown. Since the study used secondary data, several potential confounders or residual confounding (Body Mass Index (BMI), weight loss, immune recovery system (IRIS), and chronic diseases) did not investigate. In contrast, it can cause death in HIV/AIDS patients.

## CONCLUSIONS

Patients who do not adhere to medication and do not adhere to their medication appointments show a higher risk of dying than those who adhere to HIV/AIDS. Non-adherence to taking medication in the first year can be used as a marker to monitor adherence to medication and the patient's health condition in the future. Therefore, it is vital to monitor medication adherence through ART surveillance regularly. We suggest conducting a prospective cohort for further research to overcome the limitations of secondary data so that potential confounders such as Body Mass Index (BMI), weight loss, immune recovery system (IRIS), and chronic diseases can be studied.

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