Jurnal Info Kesehatan
Vol. 24, No. 3, Sept 2026, pp. 647-657
P-ISSN 0216-504X, E-ISSN 2620-536X
DOI: *10.31965/infokes.Vol24.Iss3.2456*
Journal homepage: *https://jurnal.poltekkeskupang.ac.id/index.php/infokes*

RESEARCH Open Access

The Incidence of Lost to Follow Up of People with Human Immunodeficiency Virus Undergoing Antiretroviral Therapy in Indonesia : A Systematic Review

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Received: 10 March 2026 Revised: 20 March 2026 Accepted: 15 August 2026

Abstract
Human Immunodeficiency Virus infection leads to Acquired Immunodeficiency Syndrome by progressively impairing immune system function, particularly cells responsible for immune defense. Antiretroviral therapy is the primary treatment for people living with human immunodeficiency virus and plays a crucial role in suppressing viral replication and improving survival and quality of life. However, the effectiveness of Antiretroviral therapy is highly dependent on treatment adherence and continuity of care. Loss to follow-up remains a significant challenge that undermines the success of human immunodeficiency virus treatment programs. Therefore, this study aims to assess adherence to antiretroviral therapy and to identify factors associated with loss to follow-up among people living with human immunodeficiency virus in Indonesia. This study employed a systematic review design conducted in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analyses guidelines. A comprehensive literature search was performed using three electronic databases: Google Scholar, PubMed, and ScienceDirect. Controlled and relevant keywords were applied to identify studies addressing factors related to loss to follow-up, including knowledge, social support, access to health services, perceptions and beliefs regarding antiretroviral therapy, drug side effects, and human immunodeficiency virus-related stigma. From a total of 4.353 articles retrieved, seven studies met the inclusion criteria and were synthesized. Of these, five used a cross- sectional design and two were case-control studies. The findings indicate that loss to follow-up among people living with Human Immunodeficiency Virus receiving Antiretroviral Therapy is associated with low levels of knowledge, inadequate social support, limited access to healthcare service, negative perception of antiretroviral therapy, adverse drug effects, and persistent human immunodeficiency virus-related stigma.

Keywords: HIV/AIDS, Antiretroviral therapy, Lost to follow up, Treatment adherence, People living with HIV.

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1. INTRODUCTION

Human Immunodeficiency Virus (HIV) infection and Acquired Immunodeficiency Syndrome (AIDS) remain major global public health challenges and are among the leading causes of mortality worldwide. Based on data from UNAIDS, it is known that as many as 39,9 million people worldwide have HIV in 2023 (UNAIDS, 2023). Similar to global conditions, Indonesia is one of the countries in Asia with a high prevalence of HIV cases. In Indonesia, as many as 31,564 HIV cases were found from January to June in 2024 (Kemenkes RI, 2024).

HIV is a virus that can cause AIDS by disrupting the performance of cells related to the immune system (Naimah et al., 2023; Teer et al., 2025). In the early phase of infection, individuals may experience acute retroviral syndrome, characterized by increased viral load and decreased CD4 cell count (Daud et al., 2025; Trisnashanti et al., 2025; Yuliaty et al., 2024). Without effective treatment, continued viral replication results in severe immune suppression, increasing susceptibility to opportunistic infections and other complications. Although individuals infected with HIV do not necessarily develop AIDS immediately, progressive immune deterioration due to untreated infection will eventually lead to AIDS (Aryani & Suwarni, 2021; Muhie & Tegegne, 2025). From a public health perspective, this progression underscores the importance of early diagnosis and sustained treatment to prevent disease advancement and reduce transmission.

One of the current treatments for people with HIV is antiretroviral therapy (ART). Although antiretroviral therapy has not been able to cure HIV completely, antiretroviral therapy is able to reduce mortality and morbidity, improve the quality of life of people with HIV and AIDS, and increase people's hope. Antiretroviral therapy is part of HIV and AIDS treatment that aims to reduce the risk of HIV transmission, inhibit the worsening of opportunistic infections, improve the quality of life people with HIV, and reduce the amount of virus (viral load) in the blood (Lailatussa et al., 2023). Antiretroviral therapy is given to adult HIV patients and children aged 5 (five) years and over who have shown clinical stage 3 or 4, pregnant women with HIV, babies born to mothers with HIV (Melit et al., 2025; Spielberger et al., 2025). ART also given to HIV patient with tuberculosis, HIV patient with hepatitis B and hepatitis C, HIV patients in key population, HIV patients whose partners are negative, and HIV patients in the general population living in widespread HIV epidemic areas (Denson et al., 2022; Moreno et al., 2020; Strauss et al., 2025). Principle antiretroviral administration is to use 3 types of drugs, all of which must be absorbed and in the blood dose. Clinical monitoring under the supervision of a doctor as an evaluation material must be carried out routinely at least once a month in the first 6 (six) months after the administration of antiretroviral therapy. Subsequent monitoring by a doctor can be done at least once every 3 (three) month or more frequently, according to the patient's condition and compliance with treatment (Nurur et al., 2018).

Globally, 31.6 million PLHIV had access to ART in 2024 (World Health Organization, 2025a). Although there has been an increase since 2010, this figure has not yet reached the target set for 2025, which is that 34 million HIV patients should have access to antiretroviral therapy. Antiretroviral therapy has begun to be administered to some PLHIV in Indonesia. This is evident from the Executive Report on the Development of HIV/AIDS and Sexually Transmitted Infections (STIs) in the first half of 2024, which states that 23.375 (74,1%) PLHIV in Indonesia have started antiretroviral therapy. Although the number of PLHIV receiving antiretroviral therapy has reached 74,1%, this is still below the global target of 95% of PLHIV receiving antiretroviral therapy (Kementerian Kesehatan RI, 2024).

The number of PLHIV who started antiretroviral therapy increased in 2021-2023, but based on each year's cohort, it was found that there were PLHIV who did not continue treatment and were considered lost to follow-up (LTFU) (Kemenkes, 2023). The high number of HIV cases amid the increase in the number of PLHIV receiving antiretroviral therapy is a gap that

is still often found in the community. Some people with HIV do not continue antiretroviral therapy after undergoing treatment or initial therapy. This loss to follow-up will certainly have an impact on the life expectancy of people with HIV. People with HIV without antiretroviral therapy are known to survive for 3,7 years after experiencing a CD4 count drop to less than 200/mm3 (American Chemical Society, 2022). This certainly poses a challenge in the implementation of HIV prevention in Indonesia.

Several primary studies have reported that adherence to ART and LTFU are influenced by multiple factors including demographic characteristic, clinical conditions, and health system related barriers. Recent cohort studies have identified poor adherence, incomplete patient information, and socio clinical factor as a significant predictors of LTFU (Endebu et al., 2024 ; Gebre et al., 2025). Other studies have also shown that opportunistic infections, low CD4 counts, and lack of social support contribute to disengagement from care (Alebel et al., 2022 ; Anulo et al., 2024).

However, findings across these studies remain heterogeneous and highly context specific, reflecting variation in healthcare systems, patient populations, and study setting. Furthermore, critical periods of disengagement, particularly within the first six months of ART initiation are not consistently examined across studies. In Indonesia, although individual studies have explored ART adherence and LTFU, the available evidence remains limited and fragmented. Therefore, a systematic review is needed to synthesize existing evidence and provide a comprehensive understanding of adherence patterns and factor associated with loss to follow-up among people living with HIV.

2. RESEARCH METHOD

The literature search in this systematic review was conducted using the Preferred Reporting Item for Systematic Reviews and Meta-Analysis (PRISMA) guidelines with a model shown in Figure 1.

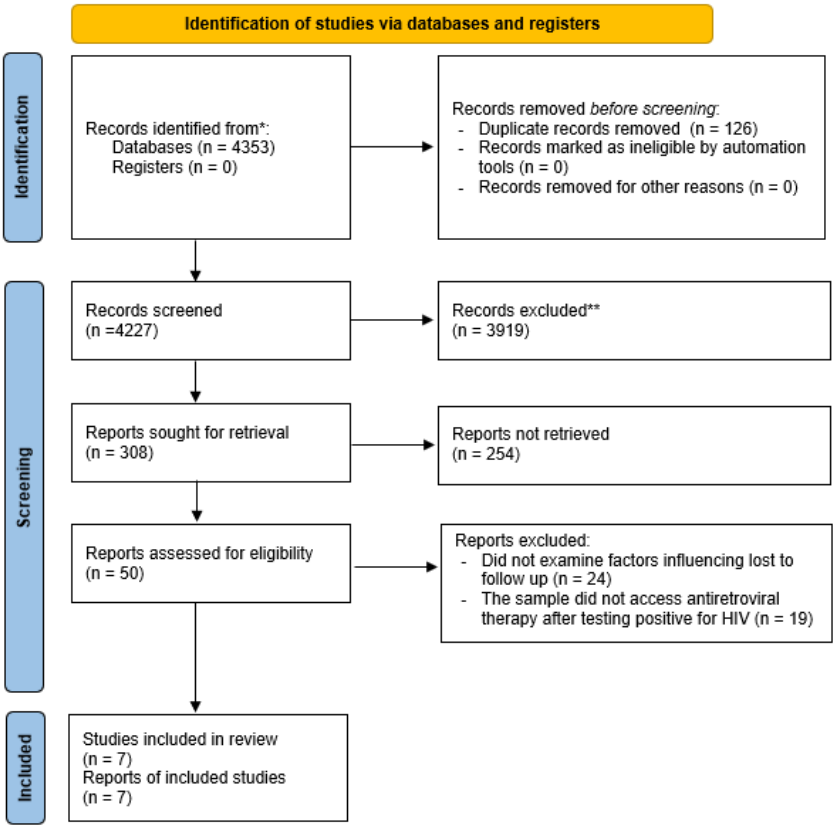


Figure 1. PRISMA flow diagram (Scientific Article Selection Process)

All record identified from the database search were exported into a reference list, and duplicate records were removed. Study selection was conducted in two stages. Initially, titles and abstracts were screened to identify potentially relevant studies. Full-text articles were then assessed against the predefined eligibility criteria. Seven studies fulfilled in the inclusion criteria and were included in the final review.

The methodological quality of the included studies was evaluated using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist according to the study design. The JBI Analytical Cross-Sectional Checklist was applied to cross-sectional studies, the JBI Case-Control Checklist to case-control studies, and the JBI Qualitative Checklist to qualitative studies. Each study was independently assessed using the appropriate checklist. Studies that fulfilled most of the appraisal criteria were considered to have acceptable methodological quality and were included in the review. The appraisal also served to identify potential sources of bias that might influence the interpretation of the findings. All included studies demonstrated acceptable methodological quality and were therefore retained for data synthesis.

The articles selected for this review are original scientific publications written in Indonesian or English and published between 2020 and 2025. The included studies used cross-sectional, case-control, with samples consisting of people living with HIV (PLHIV) who had started or were undergoing antiretroviral therapy since their initial diagnosis. Exclusion criteria were applied to articles that did not clearly describe the research methods, used samples that were not undergoing antiretroviral therapy, or did not specifically examine factors related to loss to follow-up. With there criteria, the researchers sought to ensure that only relevant studies with significant contributions were analyzed further.

This systematic literature search was conducted using three electronic databases, namely PubMed, ScienceDirect, and Google Scholar. These databases were selected because they index a wide range of international and national publications relevant to HIV care and antiretroviral therapy. The search strategy combined three main concepts such as HIV, antiretroviral therapy, and loss to follow-up. For PubMed, both Medical Subject Headings (MeSH) and free-text keywords were used to improve the sensitivity of the search. Keywords with similar meanings were combined using the Boolean operator OR, whereas different concepts were combined using AND.

The search strategy applies in PubMed was as follows: (“HIV”[MeSH] OR HIV OR “Human Immunodeficiency Virus” OR PLHIV) AND (“Antiretroviral Therapy”[MeSH] OR “antiretroviral therapy” OR ART OR ARV) AND (“Loss to Follow-Up” OR “lost to follow-up” OR LTFU OR “treatment discontinuation” OR “retention in care”) AND (knowledge OR “social support” OR stigma OR perception OR belief OR “healthcare access” OR “drug side effects”). Equivalent search strategies were adapted for ScienceDirect and Google Scholar by using the same keywords and concepts while adjusting the search syntax according to the requirements of each database.

Table 1. Methodological quality assessment of the included studies

Authors, year	Study Design	JBI Tool	Score	Overall Quality
Kurniawan et al., (2022)	Cross-sectional	JBI Cross-sectional	8/8	High
Suryana et al., (2022)	Cross-sectional	JBI Cross-sectional	8/8	High
Hutahaean et al., (2023)	Qualitative	JBI Qualitative	8/8	High
Sutini et al., (2020)	Case-control	JBI Case-control	8/8	High
Damanik et al., 2024)	Mixed-method	JBI Cross-sectional	8/8	High
Hikmah et al., (2020)	Case-control	JBI Case-control	8/8	High
Fibriansari & Cahyadi, (2021)	Cross-sectional	JBI Cross-sectional	8/8	High

Data extraction was performed using a standardized data extraction form. The extracted information included the author, year of publication, study location, study design, sample characteristics, sample size, study objectives, variables examined, methods of analysis, and the main findings related to factors associated with loss to follow-up. The extracted data were reviewed to ensure consistency before being synthesized.

The findings from the included studies were synthesized narratively. Factor associated with loss to follow-up were grouped into common themes, including patient related factors, social support, healthcare access, treatment related factors, and stigma. Similarities and differences across studies were compared to provide a comprehensive understanding of factors influencing loss to follow up among people living with HIV receiving antiretroviral therapy in Indonesia

3. RESULTS AND DISCUSSION

The total number of scientific articles obtained from a comprehensive search on Google Scholar, PubMed, and Elsevier was 4353 articles. A total of 126 studies were eliminated due to duplication, leaving 4227 scientific articles. These 4227 scientific articles were then filtered again based on inclusion and exclusion criteria, resulting in 52 scientific articles. Finally, 7 scientific papers were selected after elimination based on feasibility, inclusion criteria, and research objectives. The characteristics of the scientific articles and data extraction tables are.

Table 1. Characteristics of scientific studies

Authors, year, title	Objective	Location and Study Design	Main Findings
Kurniawan et al., (2022). Faktor-faktor determinan penyebab loss to follow up pada orang dengan HIV dan AIDS (ODHA) yang menerima terapi Antiretroviral (ARV).	To identify determinants of loss to follow up among people living with HIV receiving antiretroviral therapy.	Regional General Hospital Tangerang Regency ; Quantitative, cross-sectional	Health insurance, ARV side effects, CD4 count, family support hopelessness, stress levels, and self-esteem were identified as factors associated with loss to follow-up.
Suryana et al., (2022). Factors associated with antiretroviral therapy adherence among patients living with HIV during the COVID-19 pandemic: A cross-sectional study.	To identify factors associated with antiretroviral therapy adherence among people living with HIV during the COVID-19 pandemic.	Wangaya Regional General Hospital ; Quantitative, cross-sectional	Employment status, ART regimen, family support, and perceptions of the COVID-19 pandemic were associated with antiretroviral therapy adherence.
Hutahaean et al., (2023). Barriers and Facilitators to HIV Treatment Adherence in Indonesia: Perspectives of People Living with HIV and HIV Service Providers.	To explore barriers and facilitators to HIV treatment adherence from the perspectives of people living with HIV and HIV service providers.	Jakarta Province ; Qualitative, cross-sectional	HIV-related stigma was identified as the main barrier contributing to loss to follow-up among people living with HIV.
Sutini et al., (2020). Socio-demographic Factors Associated with Loss to Follow up Anti Retro Viral Therapy among People	To examine the association between educational level, employment status, distance to healthcare facilities, and	Semarang City ; Quantitative, case-control	Educational level, employment status, and distance to healthcare facilities were significantly associated with

Living with HIV and AIDS in Semarang City	adherence to antiretroviral therapy.		adherence to antiretroviral therapy.
Damanik et al., (2024). Evaluasi Kepatuhan dan Kedisiplinan Pengambilan Ulang Obat Antiretroviral (ARV) oleh Pasien HIV/AIDS di Sebuah Rumah Sakit Swasta Jakarta Utara Periode Tahun 2023.	To evaluate adherence to antiretroviral therapy among HIV/AIDS patients.	Hospital in Jakarta Utara Regency ; Mixed Method (quantitative & qualitative), cross-sectional	Distance to healthcare facilities, forgetfulness, inadequate family support, and perceived drug side effects contribute to poor adherence to antiretroviral therapy.
Hikmah et al., (2020). Case study of Factors Causing Lost to Follow Up of HIV Patients in Antiretroviral Treatment at Kencong Public Health Center, Jember, East Java.	To identify factors associated with loss to follow-up among HIV patients receiving antiretroviral therapy.	Kencong Community Health Center, Jember, East Java ; Qualitative, case-control	Limited knowledge about HIV was associated with loss to follow-up, resulting in poor adherence to antiretroviral therapy.
Fibriansari & Cahyadi, (2021). Lost To Follow Up Terapi Antiretroviral pada Orang Dengan HIV/AIDS di Lumajang	To identify factors associated with loss to follow-up among people living with HIV/AIDS.	Dr. Haryoto Regional General Hospital, Lumajang ; Quantitative, cross-sectional	Treatment duration, ART regimen, educational level,, patients' perceptions, social support, and adherence were associated with loss to follow-up.

Of the nine scientific articles synthesized, four were studied using a cross-sectional study design, two used a case-control study design, and two used a case study design without controls. Four studies were quantitative, four were qualitative, and one was mixed-method (quantitative and qualitative).

The study conducted by Kurniawan et al., (2022) revealed that there are several factors associated with lost to follow-up in people with HIV undergoing antiretroviral therapy, namely the use of health insurance or JKN with a p-values of 0,034; side effects of therapy with a with a p-values of 0,038; family support with a p-values of 0,022; CD4 count with a p-values of 0,017; hopelessness with a p-values of 0,012; stress level with a p-values of 0,033; and self-esteem with a p-values of 0,002. Research conducted by Suryana et al., (2022) explains other factors that influence lost to follow-up in people with HIV undergoing antiretroviral therapy, namely employment status, type of therapy given in antiretroviral therapy, social support, and limited access to health services due to the Covid-19 pandemic.

Unlike the finding Kurniawan et al. and Suryana et al., research conducted by Hutahaean et al., (2023) explains that HIV-related stigma is one of the factors that influence lost to follow-up among people with HIV undergoing antiretroviral therapy. The study conducted by Sutini et al., (2020) explains that the level of knowledge, employment status, distance from home, and health care facilities contribute to the occurrence of lost to follow-up among people with HIV. Similar to the studies conducted by Kurniawan et al. and Sutini et al., the study conducted

by Damanik et al., (2024) also explains that the distance between the patient's home and health facilities as well as the side effects of antiretroviral therapy are also factors related to lost to follow-up in people with HIV. Research conducted by Hikmah et al., (2020) explains that the level of knowledge is the main factor causing lost to follow-up in people with HIV. The same thing is also explained in a study conducted by Fibriansari & Cahyadi (2021) From this study, it is known that the level of knowledge, perceptions of antiretroviral therapy, side effects of therapy drugs, and social support are related to lost to follow-up in people with HIV.

Low of knowledge among PLHIV

Knowledge is the result of searching for or sensing a particular object. Sensing occurs through the human sense. Most human knowledge is obtained through the ears and eyes. Without knowledge, a person will not have a basis for decision-making and determining actions to deal with the problems they face (Wijayanti et al., 2024). The level of knowledge of people living with HIV (PLHIV) will have an impact on their adherence to treatment programs. Many PLHIV with low level of knowledge still have difficulty understanding HIV infection, treatment instructions and objectives, the risks and positive effects of antiretroviral therapy, and the consequences of non-adherence to antiretroviral therapy (Sutini et al., 2020). The lower the level of knowledge of PLHIV about antiretroviral therapy, the greater the risk of PLHIV experiencing lost to follow up.

Basic knowledge about HIV and AIDS is very important because it can help PLHIV to prevent and spread the HIV virus to other individuals (Hikmah et al., 2020). In Indonesia, most people living with HIV (PLHIV) do not have a clear understanding of HIV or AIDS. They believe that HIV is a dangerous disease with no known cure (Fibriansari & Cahyadi, 2021). This lack of understanding about HIV/AIDS often leads PLHIV to make the wrong decisions regarding their treatment. If PLHIV's knowledge about HIV treatment is low, then there will also be low awareness in following antiretroviral therapy and discipline subsequent examinations.

Lack of social support

Social influence or support has a significant contribution to the success of antiretroviral therapy. Social influence makes individuals feel the need or not to engage in expected or recommended behaviours (Rachmawati, 2019). Research conducted by Kurniawan et al., (2022) explains that psychological disorders are very likely to occur in PLHIV couples who have children confirmed positive for HIV. Many children with HIV experience lost to follow-up in antiretroviral therapy because they are not explained why they must take antiretroviral drugs every day. The lack of support from family members for children with HIV leads to irregularity in the individual's adherence to antiretroviral therapy.

Family support can also indirectly boost patients' self-esteem, making people with HIV more enthusiastic about undergoing antiretroviral therapy and giving them the impression that they will live longer in good health. Research conducted by Fibriansari & Cahyadi (2021) concluded that even though people with HIV who lost to follow-up on ART had received support from health workers during antiretroviral therapy, they were still irregular in undergoing antiretroviral therapy because they did not receive support from their partners or families. Families and partners play an important role in the antiretroviral therapy process. Families and partners play a role in reminding PLHIV to take their medication so that PLHIV adherence to antiretroviral therapy has increased.

Limited access to health services or VCT Clinics

The reach of health services is often associated with the ability of service users (patients) to travel the distance and time required to reach healthcare facilities. Healthcare facilities in Indonesia are not evenly distributed, so some patients living in remote areas have difficulty accessing healthcare services for themselves. Currently, the Indonesian Ministry of Health has established a regulation that each sub-district must have one community health center. However, this has not been fully implemented in Indonesia, particularly in the provinces of

Central Papua, West Papua, Southwest Papua, and Papua Pegunungan. This illustrates that access to health services, particularly primary healthcare, for the people in these provinces is still not ideal. The absence of community health centers in these subdistricts is due to difficult geographical conditions (Kementrian Kesehatan Republik Indonesia, 2023).

The majority of patients lost to follow-up studied by Sutini et al., (2020) lived more than 5 kilometers from the nearest health care facility. This meant that they had to spend more money and time traveling to the health care facility. The considerable distance from patients' homes to antiretroviral therapy health facilities also caused respondents in study by Damanik et al., (2024) to be late in taking their antiretroviral therapy medication. Distance and the cost of traveling to health facilities every month are obstacles for PLHIV in undergoing antiretroviral therapy.

PLHIV perceptions of antiretroviral therapy

Perceptions regarding the benefits of antiretroviral therapy are also one of the factors associated with loss to follow-up. Research conducted by Fibriansari & Cahyadi (2021) explains that PLHIV who do not feel the benefits will have an impact on the lack of commitment in PLHIV to undergo antiretroviral therapy regularly. Additionally, some PLHIV sometimes misinterpret the usefulness of drugs due to the side effects that arise after taking antiretroviral therapy. This condition causes a decreases in the perception of benefit for these PLHIV, which leads to non-compliance in undergoing antiretroviral therapy.

Side effects of antiretroviral therapy

Research conducted by Kurniawan et al., (2022) explains the relationship between ARV therapy side effect and lost to follow up cases in antiretroviral therapy. The number of drugs, the size of the drugs, and the time of administration consumed are obstacles for children undergoing antiretroviral therapy. Loss to follow-up in antiretroviral therapy can be due to patients feeling bored with taking medication and experiencing several side effects such as dizziness, nausea, loss of appetite, tingling, joint pain, chills, and frequent fatigue Damanik et al., (2024).

HIV-related stigma

HIV-related stigma remains a major barrier to treatment retention among people living with HIV. Fear of disclosure and discrimination discourages PLHIV from accessing healthcare services and collecting antiretroviral medications, thereby increasing the risk of loss to follow-up (Hutahaean et al., 2023).

4. CONCLUSION

Lost to follow-up among people with HIV undergoing antiretroviral therapy is associated with several factors. This is evident from the majority of scientific articles selected, which present significant results between several factors and lost to follow-up among people with HIV. The factor associated with loss to follow-up in people living with HIV undergoing antiretroviral therapy are low knowledge of HIV, lack of social support, limited access to health services, HIV perceptions of antiretroviral therapy, side effects of drug taken during antiretroviral therapy, and HIV related stigma. The presence of social support and health workers in motivating PLHIV can indirectly reduce the incidence of lost to follow-up. Therefore, cooperation between several parties is needed, including immediate family, peers, and health workers who are able to explain in more detail the benefits of antiretroviral therapy so that PLHIV are more confident and enthusiastic in undergoing treatment.

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