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Cost-Effective Analysis (AEB) of Antiretroviral (ARV) Use of TLD and TLE in Outpatient HIV Patients

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ABSTRACT

Antiretroviral treatment is one of the biggest parts of the treatment for people infected with HIV. This study aims to determine the effectiveness of drugs and the cost efficiency of ARV combination drug therapy. The study used a non-experimental research design that was observational to determine the Cost Effectiveness Analysis of 2 combinations of ARVs, namely the combination of TLD (Tenofovir + Lamivudin + Dolutegraph), and the combination of TLE (Tenofovir + Lamivudin + Efavirenz). Data collection was carried out retrospectively from the medical record data of patients who started ARV treatment in the period 2021 to 2023. Total of 189 patients were actively treated as outpatients at VCT polyclinics and 64 who met the inclusion criteria were used as study subjects. The effectiveness of treatment uses the parameters of the Viral Load test results. Treatment is said to be effective if the Viral Load test result is <40 copies/mL. Based on the results of the Viral Load test, the TLD combination was more effective (75.9%) compared to the TLE combination (66.7%). Based on Cost Effective Analysis, the combination of TLD (Tenofovir + Lamivudin + Dolutegrafir) is better with an ACER value of IDR 39,871 compared to the combination of TLE (Tenofovir + Lamivudin + Efavirenz) with an ACER value of IDR 68,599.

Keywords: HIV; AIDS; effectiveness; pharmacoeconomics; cost effective analysis; viral load

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INTRODUCTION

Human Immunodeficiency Virus (HIV) is a virus that can weaken the human immune system. HIV can cause *Acquired Immuno-Deficiency Syndrome* (AIDS), which is a condition in which the immune system is so weak that the body is susceptible to various infections and serious diseases. Therefore, countermeasures are needed to prevent and control the spread of HIV, AIDS, and STIs (Ministry of Health of the Republic of Indonesia, 2022b).

According to data from, it is estimated that there are 543,100 people in Indonesia infected with HIV/AIDS. A total of 30,137 people died from AIDS in the same year. Of the number of people living with HIV in Indonesia, as many as 149,883 people have received antiretroviral treatment (ARV). Ministry of Health of the Republic of Indonesia (2023) Based on data from, the number of new HIV cases in Jambi Province shows an up-and-down trend from 2018 to 2022. In 2018, there were 125 cases, increased to 183 cases in 2019, and decreased to 169 cases in 2020. Then there was an increase in 2021 to 186 cases and 227 in 2022. The number of people living with HIV in 2022 is estimated at 3,741 people. Jambi Provincial Health Office (2022)

Cost-Effectiveness Analysis (AEB) is a method to assist decision-making in choosing the best program or drug among several options with the same goal. AEB works by converting cost and effectiveness into a ratio of antiretroviral treatment (ARV) to being one of the largest

parts of the treatment for people living with HIV. Research conducted by (Faridah et al., 2016). Hardjadipura et al., (2018) shows that the cost of using ARVs ranges from IDR 4,281,948 to IDR 4,680,000. This is a relatively large cost. Therefore, it is necessary to make efforts to calculate the cost and effectiveness of HIV treatment.

In a previous study conducted by Anggriani et al., (2020) a Cost-Effective Analysis (AEB) of Combination Treatment of Zidovudin, Lamivudine, Nevirapin and Combination of Tenofovir, Lamivudine, Efavirenz (TLE) in HIV/AIDS Patients at Bekasi City Hospital, the results were obtained that the combination of Tenofovir, Lamivudine, and Efavirenz (TLE) was more effective than the combination of Zidovudin, Lamivudine, and Nevirapin with a cost-effectiveness ratio (ACER) in HAART A of 16,227.4, while the effective ratio of HAART B cost bags (ACER) was 28,330.7.

This study has novelty in integrating the latest data on HIV case trends in Jambi Province (Jambi Provincial Health Office, 2022) with an analysis of the cost-effectiveness of antiretroviral (ARV) treatment. Unlike previous studies that only compared the cost-effectiveness ratio between ARV combinations (Anggriani et al., 2020), this study combines national (Ministry of Health RI, 2023) and regional epidemiological data, and applies the Cost-Effectiveness Analysis (AEB) method to get a more comprehensive picture of the burden of HIV treatment costs. This innovation is expected to produce recommendations for more targeted treatment strategies amid limited resources.

The purpose of this study is to evaluate the cost-effectiveness comparison between two combinations of ARV treatment, namely the combination of Tenofovir, Lamivudine, and Efavirenz (TLE) and the combination of Zidovudin, Lamivudine, and Nevirapin, identify the factors that affect the cost and effectiveness of treatment, and provide evidence for optimizing budget allocation and improving HIV/AIDS management programs at the national and regional levels. The benefits of this research can be used as a reference for the government and policymakers in designing more efficient strategies for managing HIV/AIDS program funds, helping health institutions improve the effectiveness of services and treatment, and improving access and quality of treatment for ODHA so that the death rate due to AIDS can be reduced, so that overall it has an impact on improving community welfare.

METHOD

This study uses a non-experimental research design that is observational. The object used is patient medical record data taken at the Simpang Kawat Health Center in Jambi City retrospectively. The method used to determine the sample used in this study is *purposive sampling*. The determination of this sample is based on the purpose of the study. The sample in this study is outpatient HIV patients at the Simpang Kawat Health Center, Jambi City who meet the inclusion criteria.

The inclusion criteria in this study include:

1. Outpatient HIV patients at the Simpang Kawat Health Center, Jambi City, who started therapy in 2021 – 2023.
2. Patients who received Antiretroviral (ARV) combination TLD (Tenofovir, Lamivudine, and Dolutegravir) and TLE (Tenofovir, Lamivudine, and Efavirenz).
3. Patients who have data on the results of *the Viral Load* (VL) level test.

Data Processing and Analysis

1. Patient demographic data including age and gender are presented in the form of a frequency distribution table.
2. Treatment data are presented in the form of frequency distribution tables.
3. Calculation of the total average cost which is the sum of the medical expenses and laboratory costs.
4. Calculation of treatment effectiveness.
   The analysis of the effectiveness of the use of antiretroviral drugs was carried out to determine the effectiveness of the use of the drug in HIV patients by looking at the examination of *Viral Load* levels as an indicator. The percentage of therapy effectiveness can be calculated using the following formula:
   % Therapy effectiveness = $\frac{a}{b} \times 100\%$
   Information:
   a = Number of treatments that reach the target
   b = Number of patients
5. ACER and ICER value calculation
   a. ACER
   $$\frac{Rata - rata\ biaya}{\%\ efektivitas}$$
   b. ICER
   $$\frac{(Rata - rata\ biaya\ A) - (Rata - rata\ biaya\ B)}{(\%\ efektivitas\ A) - (\%\ Efektivitas\ B)}$$

RESULTS AND DISCUSSION

Patient Characteristics

Table 1. Characteristic

Characteristic	n=64	Percentage (%)
Gender		
Male	58	90,6
Woman	64	9,4
Age		
17 – 25 years old (Late Teens)	18	28,1
26 – 35 years old (Early Adult)	29	45,3
36 – 45 years old (Late adult)	9	14,1
46 – 55 years old (Early Senior)	7	10,9
56 – 65 years old (Late Elderly)	1	1,6
>65 Years (Senior)	0	0
Types of Therapy		
TLD	58	90,6
TLE	6	9,4

The distribution of patient characteristics in table 1 above shows that the most patients are male, namely 58 patients (90.6%). Furthermore, the majority of patients are in the age range of 26 – 35 years (45.3%). For treatment therapy, more patients use antiretroviral TLDs, which is 58 patients (90.6%).

Direct Medical Costs

Table 2. Average Direct Medical Costs

Type of Drug	Medicine (Rp)	Laboratory (Rp)	Consultation (Rp)	Total (Rp)
TLD	1.165.345	1.800.000	60.879	3.026.224
TLE	2.640.567	1.800.000	135.000	3.239.200

An overview of the average total cost of patients while undergoing treatment at the Simpang Kawat Health Center, Jambi City.

Drug Effectiveness Analysis

Table 3. Drug Effectiveness Analysis

Type of Drug	Viral Load *Test Results*		n = 64	Percentage Effectiveness (%)
	Effective	Ineffective		
TLD	44	14	58	75,9
TLE	4	2	6	66,7

The analysis of antiretroviral effectiveness can be seen from the test results showing a result of <40 or undetected. Based on table 3, TLDs have a higher percentage of effectiveness than TLE.

Cost-Effectiveness Analysis

Table 4. Cost-Effectiveness Analysis

Type of Drug	Average Direct Medical Costs (Rp)	Percentage of Effectiveness (%)	ACER (Rp)
TLD	3.026.224	75,9	39.871
TLE	3.239.200	66,7	48.564

Based on Table 4, it is obtained from *the calculation of ACER* Antiretroviral TLD has a lower value. This means that TLDs are more *cost-effective.*

Patient Characteristics

1. Age

According to the Ministry of Health of the Republic of Indonesia in 2009, age is categorized as late adolescence 17 – 25 years old, early adulthood 26 – 35 years, late adulthood 36 – 45 years, elderly age 46 – 65 years, and seniority over 65 years. Based on the results obtained, most of the patients were in early adulthood or in the age range of 26 – 35 years, which was 29 patients (45.3%).

This is in line with research conducted by Anggriani et al., (2020) and which shows that the most people with HIV are in early adulthood or at the age of 26-35 years. Based on the report Fitrianingsih et al., (2019) (Ministry of Health of the Republic of Indonesia, 2022a) on the number of ODHIV found in the period January – March 2022, most of them are also found in the age group of 25 - 49 years (67.9%). According to researchers, people in the age group of 26 to 35 years are more susceptible to HIV infection because in this age group they are more active in sexual activity and engage in behaviors that can increase HIV transmission, such as having sex without a condom and changing partners. In addition, this age group has high mobility.

2. Gender

Based on gender, most HIV patients are men rather than women. The number of male patients was 58 patients with a percentage of 91% and 6 female patients with a percentage of 9%. The results of this study are in line with research conducted by (Novrindo Sidjabat et al., 2019) the Gambiran Regional General Hospital, Kediri City, namely People with HIV/AIDS (ODHA) with more male gender with a percentage of 64.2% compared to women with a percentage of 35.8%. According to the Ministry of Health of the Republic of Indonesia (2022a) report on the number of People With HIV (ODHIV) found in the period January – March 2022, most of them are found in the age group of 25 - 49 years (67.9%) and male (71%).

According to men, they are susceptible to HIV infection, this is due to negative behaviors such as using syringes, buying sex services, and men who are far from their partners so they have high mobility. In addition, Umam et al., (2015) Claudia et al., (2018) it states that one of the factors that causes men to be more susceptible to HIV infection is sexual intercourse with men through anal (*Homosexual*). *Homosexuality* is a sex that is very risky to transmit HIV, this is because the anus is not used for sexual intercourse so that it will cause injuries and facilitate the entry of the HIV virus into the body. Meanwhile, women are more likely to contract HIV from their sexual partners. (Sidjabat et al., 2016)

3. Antiretroviral Therapy

The antiretroviral therapies used are TLD (Tenofovir, Lamivudine, and Dolutegravir) and TLE (Tenofovir, Lamivudine, and Efavirenz). There were 58 patients with a percentage of 90.6% and 6 patients with a percentage of TLD with a percentage of 9.4%. This happens because TLDs have better effectiveness than TLE. In addition, TLD also has fewer side effects compared to TLE. However, in this study, there are still patients who use TLE, because patients feel comfortable with antiretroviral TLE. In addition, patients with comorbidities with tuberculosis who take Rifampicin are more recommended to use TLE because Efavirenz is more compatible with Rifampicin.

According to (Ministry of Health of the Republic of Indonesia, 2019) TLD, it has 3 ingredients, namely Tenofovir 300mg, Lamivudine 300mg, and Dolutegraphir 50mg. The combination is consumed 1x a day 1 tablet. (World Health Organization, 2019) Dolutegravir is an integrase inhibitor (INSTI), which works by preventing the HIV virus from joining the DNA of the host cell. NRTI (Tenofovir and Lamivudine) works by inhibiting the enzyme reverse transcriptase, an enzyme that the HIV virus needs to multiply. This enzyme converts viral RNA into DNA, which is then incorporated into the

DNA of human cells. By inhibiting this enzyme, NRTI can prevent the HIV virus from multiplying and infecting new cells (Cottrell et al., 2013) .

TLD is currently recommended as a first-line regimen for ODHA who are just starting ART, while TLE is recommended as a second-line regimen. The combination of DTG with 2NRTI as the first line of research may better suppress viral numbers and reduce the risk of drug-drug interactions, therapy discontinuation, and drug resistance compared to EFV-based (World Health Organization, 2019) (Cottrell et al., 2013) regimens. *The risk-benefit* model shows that the benefits of DTG for pregnant women are greater in reducing the number of viruses, the number of maternal deaths is less, and the number of sexual transmission and mother-to-child transmission is less, compared to the risks, such as morbidity due to weight gain related to DTG (Dugdale et al., 2019).

Every ARV has toxicity, as well as DTG. Toxicity can occur in the first few weeks after initiation or up to prolonged use. DTG toxicity is a neuropsychiatric, gastrointestinal, hepatotoxic, hypersensitivity, and weight gain disorder. Neuropsychiatric disorders due to DTG are reported to be mild and rare, unlike in the use of efavirenz. However, weight gain is indeed seen in the use of DTG. Therefore, in ODHA with weight gain, it is also necessary to consult a nutrition specialist, without having to substitute from DTG to other ARVs (World Health Organization, 2019) .

Compared to other viruses, HIV is more susceptible to drug resistance. *The genetic barrier to resistance* in DTG is higher than that of ART in the NNRTI or NRTI groups. *The genetic barrier to resistance* indicates the number of mutations in the target of the ARV therapy that are required to cause a clinically meaningful loss of ability to the drug. (Clutter et al., 2016)

Direct Medical Costs

Direct medical costs are costs that must be paid for health services. These costs include medical expenses, medical personnel, laboratory test costs, and cost of monitoring effectiveness and side effects. Direct medical costs are calculated from the total average cost of HIV patients. In this study, the direct medical costs used are drug costs, laboratory costs, and consultation costs. The average direct medical cost for patients with antiretroviral TLD was Rp3,026,224 while for patients with antiretroviral TLE was Rp3,239,200. (Ministry of Health of the Republic of Indonesia, 2013)

Laboratory fees are the cost of supporting patient examinations, namely checking HIV virus levels in the blood. The laboratory fee for each patient is IDR 1,800,000. Furthermore, the consultation fee for each patient is IDR 5,000. This consultation is carried out every month when the patient takes monthly medication. This consultation was carried out with the aim of monitoring the effects of therapy and side effects of the drugs used. In addition, this consultation also aims to increase patient compliance in consuming drugs that are useful to improve the patient's quality of life.

Drug Effectiveness Analysis

The analysis of drug effectiveness is carried out by looking at HIV treatment parameters, namely checking the level *of Viral Load* (VL) in the blood. *Viral Load* (VL) is the amount of HIV virus in the blood which is then expressed as a unit of copies in one milliliter (ml) of blood. The *Viral Load* (VL) test is a test that aims to find out or measure the amount of HIV virus in the blood. Treatment is said to be effective if the level *of Viral Load*

in the patient's blood is less than 40 *copies*/mL According to (Ministry of Health of the Republic of Indonesia, 2019). (Dewanti & Handayani, 2021) the Viral *Load* test , it is the most effective method and the main standard for controlling or monitoring People With HIV and AIDS (ODHA) who are undergoing treatment. The *Viral Load* rate of ≤ 10,000 is categorized as low and *the Viral Load* rate of ≥ 100,000 is categorized as high. Then the *level of Viral Load* ≤ 40 is said to be undetectable. (Ministry of Health of the Republic of Indonesia, 2019)

From the data obtained, there were 48 out of 64 patients (75%) with effective treatment. Among them were 44 patients out of 58 patients with the use of antiretroviral TLD and 4 patients out of 6 patients with the use of antiretroviral TLD. This shows that treatment with antiretroviral TLD is more effective than treatment with antiretrovital TLE. This is because antiretroviral TLD has more advantages than antiretroviral TLE. Among them, antiretroviral TLDs have a low risk of drug resistance, minimal side effects, and low drug interactions (Dugdale et al., 2019).

Cost-Effectiveness Analysis

Cost-Effectiveness Analysis (AEB) is a method to assist decision-making in choosing the best program or drug among several options with the same goal. AEB works by converting cost and effectiveness into a ratio Cost Effectiveness Analysis (AEB) is described in the form of a ratio, both with (Ministry of Health of the Republic of Indonesia, 2013). *the Avarage Cost Ratio (*ACER) and *Incremental Cost Effectiveness Ratio* (ICER). ACER is the amount of cost needed to improve *the outcome* of a treatment (Faridah et al., 2016).

In this study, a comparison of treatment costs with antiretrovirals TLD and TLE was carried out. The ACER value from the use of antiretroviral TLDs was Rp39,871 per increase in effectiveness, while the use of antiretroviral TLEs was Rp48,564 per increase in effectiveness as listed in table 4 This shows that the use of antiretroviral TLDs is more effective and efficient than the use of antiretroviral TLDs. This is shown by the ACER value of the use of antiretroviral TLDs is lower than the use of antiretroviral TLEs and with a percentage of effectiveness of antiretroviral use of TLDs is better than the use of antiretroviral TLEs which can be seen in table 3. From these results, ICER calculations are not needed in this study.

CONCLUSION

Based on the results of this study, it can be concluded that the use of antiretroviral TLDs (Tenofovir, Lamivudine, and Dolutegravir) is more dominant than antiretroviral TLEs (Tenofovir, Lamivudine, and Efavirenz), with a total of 58 patients (90.6%) for the TLD regimen and 6 patients (9.4%) for the TLE regimen. In addition, in terms of effectiveness and cost efficiency, antiretroviral TLD showed superior results with an effectiveness rate of 75.9% based on the results of the Viral Load test and an Average Cost-Effectiveness Ratio (ACER) value of Rp39,871, compared to antiretroviral TLE which had an effectiveness of 66.7% and an ACER value of Rp68,599. These results showed that the TLD regimen was more cost-effective compared to TLE in the treatment of patients undergoing antiretroviral therapy. So that it can be a more optimal choice in treatment strategies. These findings can be a basis for consideration for medical personnel and policymakers in determining a more effective and efficient therapy regimen for patients receiving antiretroviral therapy.

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