



# Cost-Effectiveness of Oseltamivir and Favipiravir in Covid-19 Patients: a Cost-Effectiveness Analysis Study in a Hospital

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**ABSTRACT:** The COVID-19 pandemic poses not only a threat to health but also to the global economy, including healthcare costs. Although there is no specific drug for COVID-19 patients, there are antiviral drugs such as oseltamivir and favipiravir that can be used to treat COVID-19. The purpose of this study was to determine the most cost-effective antiviral therapy between oseltamivir and favipiravir for COVID-19 patients in one of the hospitals in Banten province. The pharmacoeconomic method used in this study was cost-effectiveness analysis by calculating the Average Cost-Effectiveness Ratio (ACER) and Incremental Cost-Effectiveness Ratio (ICER). The results of this study showed that the ACER value of the favipiravir group (IDR 364,010 (n = 7)) was lower than the oseltamivir group (IDR 431,744 (n = 7)), with an ICER value of IDR 60,605. Based on the results of the Mann-Whitney test, there was no significant difference between the costs of the favipiravir and oseltamivir groups (p value 0.940). The sensitivity test showed that the cost of medical consumables was the cost that had the greatest impact on cost-effectiveness. Based on the calculation results, it can be concluded that the favipiravir group is more cost-effective than the oseltamivir group.

**Keywords:** oseltamivir; favipiravir; COVID-19; hospital..

## Introduction

COVID-19 is a respiratory disease caused by infection with severe acute respiratory syndrome coronavirus 2 (SARSCoV-2). The SARSCoV-2 virus is one of the newly identified variants of the coronavirus. COVID-19 was first identified in Indonesia in early March. As of June 21, 2020, the number of positive COVID-19 cases was recorded at 46,845 cases with 25,000 deaths [1]. In 2021, the number of reported COVID-19 cases increased to 907,929 cases, with 25,987 deaths due to COVID-19 [2].

Until now, specific treatment for COVID-19 disease has not been found [3]. In 2020, WHO reported that several drugs have the potential to be used in the treatment of COVID-19 based on trial results that showed good effectiveness. The solidarity clinical trial activities coordinated by WHO were followed by several countries, with the aim of testing a number of candidate drugs in the treatment of COVID-19 [4,5].

The cost of treating infectious diseases in hospitals can be offset through requests to the government. Therefore, adjustments to departmental instructions are needed. Decree of the Minister of Health Number HK.01.07/MENKES/446/2020 concerning Technical Guidelines for Claims for Certain New Patients with

Infectious Diseases in hospitals that provide services for Coronavirus disease (COVID-19) needs to be adjusted to developments in laws and regulations. This adjustment aims to meet technical claim requirements and support health services provided to COVID-19 patients [6].

Clinical administration services in hospitals need to be improved by providing equipment and facilities that meet standards. The need for special isolation rooms, medical procedures, and the use of drugs in the treatment of COVID-19 patients in hospitals requires relatively high costs [7]. This condition shows the importance of carrying out pharmacoeconomic evaluations using cost-effectiveness analysis methods to determine the extent to which the costs incurred provide effectiveness in patient care [8]. Therefore, the aim of this study was to identify the most cost-effective therapy between oseltamivir and favipiravir in COVID-19 patients at one of the hospitals in Tangerang Regency.

## Methods

### Research Design

This study used a non-experimental observational design with a cross-sectional approach.

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Data were collected through a retrospective purposive sampling method. Purposive sampling is a sampling technique that is carried out based on certain criteria that have been determined by the researcher [9].

### Population and Sample

The population in this study included data on COVID-19 patients hospitalized at Hospital X in Tangerang Regency during the period from June to December 2021. The study sample consisted of patients who met the inclusion and exclusion criteria. The inclusion criteria included patients aged 18-64 years, patients using oseltamivir or favipiravir, patients who were allowed to go home by a doctor, and patients with complete medical record data and cost data. Meanwhile, the exclusion criteria included patients who died or were forcibly discharged, patients with incomplete medical record data and costs, patients treated in the ICU, and patients who experienced a switch in antiviral therapy from oseltamivir to favipiravir or vice versa.

### The Basis of Therapy Effectiveness

COVID-19 is a disease that affects the respiratory tract, so it is closely related to oxygen saturation. COVID-19 patients, especially those with moderate to severe degrees, require hospitalization. In this study, the effectiveness of therapy was assessed based on the length of stay (LOS) and oxygen saturation percentage, which are important indicators in assessing patient care outcomes.

Length of stay (LOS) for inpatients is the total duration of a patient's hospitalization in days. This calculation is calculated from the first day the patient is admitted to the last day the patient completes his/her hospitalization in the hospital [10]. Length of stay (LOS) can be used as an indicator of the quality of health services in a hospital. The lower the LOS value, the better the quality of health services in the hospital, because it shows efficiency in managing patient care [11]. This can be influenced by the selection or determination of the therapy pattern used. Based on research conducted by Ndaparoka et al., (2021) regarding the Average Length of Stay (AVLOS) of COVID-19 patients in hospitals, the results of the study showed that the ideal LOS standard for COVID-19 patients is less than 15 days. Therefore, in this study, patients who are considered effective are patients with a LOS value of less than 15 days [12].

Oxygen saturation is the level of oxygen in the blood that binds to hemoglobin. This parameter can be used to measure the level of damage to vital organs in the human body, and in severe conditions, can cause death

due to lack of oxygen [13,14]. Generally, COVID-19 patients have oxygen saturation below 95% (normally 95-100%), which can cause hypoxia or lack of oxygen. This condition requires immediate medical attention to prevent more serious complications [15,16]. Therefore, patients with oxygen saturation values of more than 95% can be considered effective based on oxygen saturation parameters. Based on these two parameters, namely length of stay below 15 days and oxygen saturation of more than 95%, patients can be declared effective in this study.

### Data Analysis

#### *Cost Effectiveness Analysis*

The most cost-effective therapy is the therapy that has a high level of effectiveness with the lowest cost [17]. This can be measured through the ACER calculation. ACER or Average Cost-Effectiveness Ratio is a comparison between the total cost of treatment and the effectiveness of the therapy. The therapy that has the lowest ACER value compared to other therapies can be considered the most cost-effective therapy [18].

#### *Deterministic Sensitivity Analysis*

Deterministic sensitivity analysis is performed to address the uncertainties that may occur during the calculation. In addition, sensitivity analysis is also used to determine the factors that affect the ICER calculation. Changes in price or use of health interventions are some examples of uncertainties that may occur. In this study, the results of the sensitivity analysis are presented in the form of a tornado diagram [19]. Costs and effectiveness are varied for use in sensitivity analysis [20]. Variations in one of the cost variable values with a range of  $\pm 25\%$  can be applied to deterministic sensitivity analysis [21]. If one of the variables changes in value, then the value of the other variable remains constant [22].

## Result and Discussion

The characteristics of patients in this study were based on gender and age, which are presented in [Table 1](#). The number of male and female patients respectively were 9 patients (64%) and 5 patients (36%). These data indicate that the majority of the samples were male. In addition, this study was also dominated by patients aged 40-50 years and 51-61 years, each with a percentage of 36%.

In this study, there were more male patients than female patients. This data is in accordance with data from a study conducted by Hardani et al., (2023) which showed that the number of COVID-19 patients in a public hospital

**Table 1.** Baseline characteristics of patients.

No.	Characteristics	Frequency	
		Amount	Percentage
1	Gender		
	Male	9	64%
	Female	5	36%
	Total	14	100%
2	Age		
	18-28 Years	1	7%
	29-39 Years	3	21%
	40-50 Years	5	36%
	51-64 Years	5	36%
	Total	14	100%

in Palu City with male gender (51%) was higher than female (49%). Male gender is one of the risk factors for exposure to COVID-19, because men have higher levels of enzymes in the blood than women. In addition, women have the X chromosome and sex hormones which play an important role in the formation of innate and adaptive immunity so that women are more protected than men [24].

Data collection in this study was based on age, patients who could be used as samples, namely patients with an age range of 18-64 years. This study shows that the age group of COVID-19 patients who were hospitalized in one of the Tangerang district hospitals in the period June-December 2021 was the highest, namely 40-50 years and

51-64 years. This data is in accordance with Handayani's research (2020) which shows that the most COVID-19 patients are aged 60-69 years [24].

Age is one of the risk factors for contracting COVID-19. Individuals over the age of 60 are at greater risk of exposure to COVID-19. A person over the age of 60 will experience decreased tissue and organ function, making them more susceptible to disease. In addition to decreased body function, a person over the age of 60 will also experience decreased immunity [24].

The highest average unit cost, both in the oseltamivir and favipiravir groups, was the cost of using Medical Consumables, which reached up to 10 million rupiah. For

**Table 2.** Average total cost for each cost unit.

Unit Cost	Oseltamivir Group	Favipiravir Group
Consultation and Visit	IDR 3,030,000	IDR 2,825,000
Laboratory	IDR 3,034,064	IDR 2,406,555
Radiology	IDR 102,857	IDR 154,286
Actions and Therapy	IDR 3,144,921	IDR 3,330,788
Drug	IDR 6,059,430	IDR 7,216,396
Medical Consumables	IDR 10,691,874	IDR 10,344,880
Equipment Rental	IDR 1,115,714	IDR 867,143
Other Services and Fees	IDR 566,357	IDR 655,071
Room Rental	IDR 2,908,571	IDR 3,199,286
Total	IDR 30,653,790	IDR 31,562,870
<i>p-Value</i>	0.940	

**Table 3.** Effectiveness analysis in COVID-19 patients.

Group	Length of Stay				Oxygen Saturation				Effectiveness			
	Effective (<15 Days)		Ineffective (>15 Days)		Effective (>92%)		Ineffective (<92%)		Effective		Ineffective	
	n	%	n	%	n	%	n	%	n	%	n	%
Oseltamivir	5	71%	2	29%	7	100%	0	0%	5	71%	2	29%
Favipiravir	6	86%	1	14%	7	100%	0	0%	6	86%	1	14%
p-Value	1.000				0.662				-			

the cost of using drugs, the favipiravir group had a higher nominal cost compared to the oseltamivir group, with a difference of IDR 1,156,966.

In this study, the highest average total cost was the group of COVID-19 patients using favipiravir therapy with an average cost of IDR 31,562,870. Meanwhile, the group of COVID-19 patients using oseltamivir therapy had an average total cost of IDR 30,653,790.

In this study, the effectiveness of therapy was measured based on the length of stay (LoS) and oxygen saturation. The average duration of hospitalization of COVID-19 patients was 15 days, as shown in a study by Ndaparoka et al. (2021) [12]. Based on these criteria, patients were declared effective if they had a LoS value of less than 15 days. In Table 3, the results show that based on the effectiveness of LoS, the favipiravir group had 6 patients who were declared effective, while the oseltamivir group had 5 patients who were effective.

The majority of COVID-19 patients with oxygen saturation <93% require oxygen therapy to achieve the target oxygen saturation of 92%-96% [25]. Therefore, in this study, patients were considered effective if their final oxygen saturation, or when discharged by the doctor, reached more than 92%. Based on Table 3, both groups

in this study showed the same level of effectiveness, which was 100%.

Based on the description above, in this study, samples were considered effective if they had a LoS value of less than 15 days and achieved a target oxygen saturation of more than 92%. These results indicate that the favipiravir group has a higher effectiveness compared to the oseltamivir group. However, SPSS analysis using the Mann-Whitney test showed a significance value for the oseltamivir and favipiravir groups of  $p = 1.000$  and  $p = 0.662 (> 0.05)$ , respectively. Thus, it can be concluded that there is no statistically significant difference between the LoS value and final oxygen saturation in COVID-19 patients using oseltamivir and favipiravir therapy.

LoS can be used as one of the factors that can affect the total cost of a treatment or intervention in a health facility. The longer a patient is hospitalized, the more resources are needed, such as actions, drugs, medical materials, examinations and medical personnel services, so that the total costs that must be paid will increase [26]. This study can show that the group of COVID-19 patients using favipiravir therapy has a higher effectiveness value than the oseltamivir therapy group based on the LoS value.

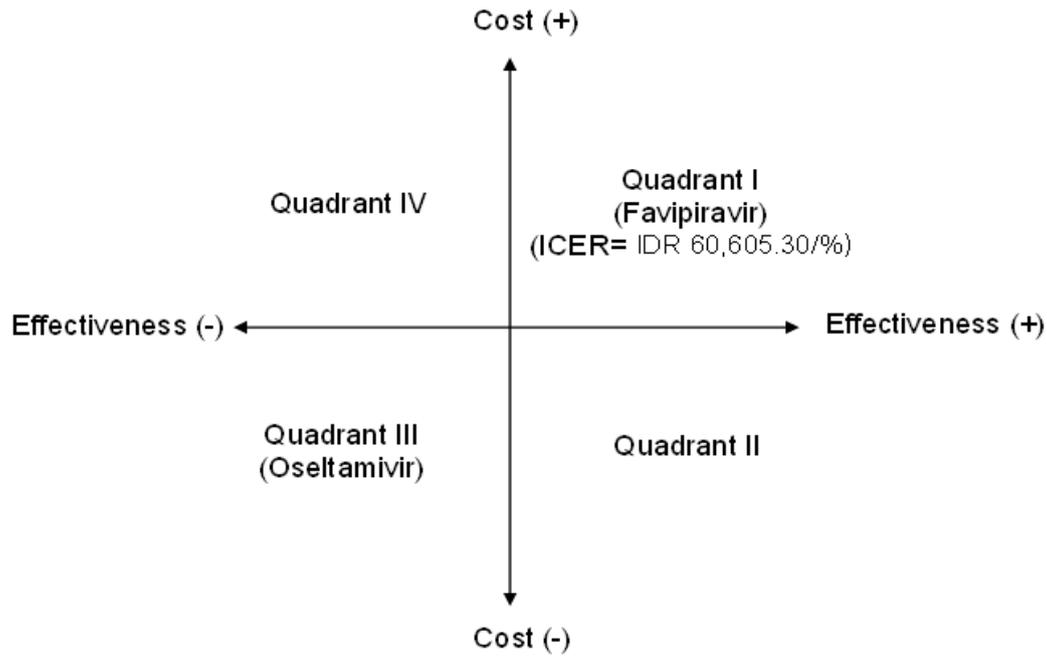
Based on research conducted by Fata and Febriana

**Table 4.** Average Cost-Effectiveness ratio (ACER) analysis.

Group	Average Total Cost	Effectiveness	ACER
Oseltamivir	IDR 30,653,790	71%	IDR 431,744
Favipiravir	IDR 31,562,870	86%	IDR 367,010

**Table 5.** Incremental Cost-Effectiveness ratio (ICER) analysis.

Group	Average Total Cost Difference	Effectiveness Difference	ICER
Favipiravir-Oseltamivir	IDR 909.079	15%	IDR 60,605.30/%



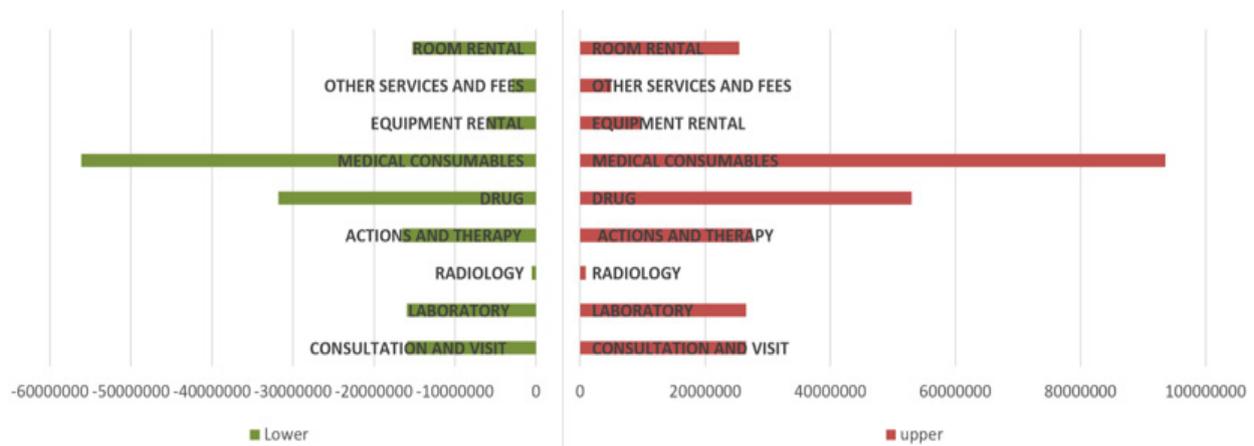
**Figure 1.** Cost effectiveness quadrant.

(2021), it showed a decrease in oxygen saturation in COVID-19 patients. This study showed that all patients achieved the target oxygen saturation value (100%) in both the oseltamivir and favipiravir groups. Patients who can be declared effective are patients who have effective status in all effectiveness parameters in this study. The results of the effectiveness analysis showed that the favipiravir group had a higher effectiveness value compared to the oseltamivir group with a difference of 15% [27].

The most cost-effective intervention is the intervention with the lowest ACER value compared to

other interventions [28]. Based on these calculations, the results of the ACER value in this study can be seen in Table 4, which shows that the favipiravir group has an ACER value of IDR 367,010, lower than the oseltamivir group which has an ACER value of IDR 431,744.

The lower the ACER of a therapy, the more cost-effective the therapy is [28]. Therefore, favipiravir is more cost-effective than oseltamivir. The results of this study indicate that although the average cost of favipiravir is higher than oseltamivir, it does not mean that oseltamivir is more cost-effective because the effectiveness value



**Figure 2.** Tornado diagram of oseltamivir sensitivity analysis.

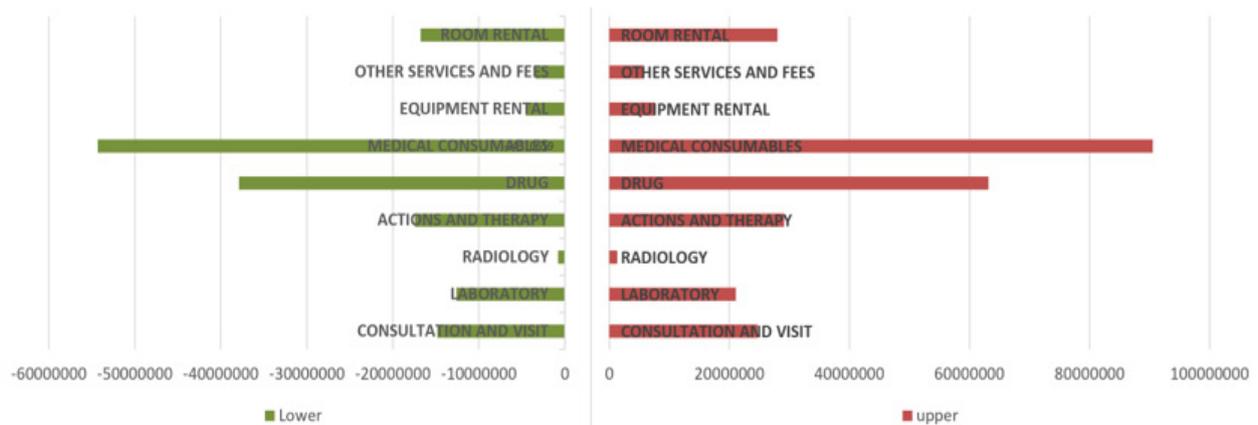


Figure 3. Tornado diagram of favipiravir sensitivity analysis.

of favipiravir is higher than the effectiveness value of oseltamivir. Based on the results of the ICER calculation, if a patient using oseltamivir wants to switch to using the antiviral favipiravir, they will be able to save costs of IDR 60,605.30.

Figure 1 shows that the favipiravir group is in quadrant I, with a higher average total cost but also higher effectiveness. Meanwhile, the oseltamivir group is in quadrant III, with a lower average total cost but also lower effectiveness [28]. Therefore, further consideration is needed through the ICER calculation. The ICER calculation is carried out to determine the additional costs that need to be incurred if the intervention is changed. Based on Table 5, it is known that if COVID-19 patients using oseltamivir therapy switch to favipiravir to increase the effectiveness of healing, an additional cost of IDR 60,605.30 per day of hospitalization is required.

The results of the sensitivity analysis show the lower limit and upper limit values. A longer range between the lower limit and upper limit indicates a greater influence on the ICER value. In this study, the parameters that provided the longest range were the cost of using Medical Consumables and the cost of using drugs, both in the oseltamivir group and the favipiravir group, as shown in Figure 2 and Figure 3.

Sensitivity analysis is performed to take into account the uncertainty aspect of various data used including the results. The emergence of uncertainty can be caused by the availability of insufficient data causing the prediction results to be less precise and accurate. In general, the results of research on parameters are in the form of discrete values (single points, for example averages) but in reality these parameters are in the form of continuous values that are randomly distributed in a certain range and

the analysis model used is related to the combination of parameters and the generalization of research results and to determine the most dominant parameters in the analysis results. The analysis is performed by calculating the upper limit and lower limit on the average of the effectiveness of each treatment [29].

Based on the sensitivity analysis, the results with the largest number of variables are the variables that have the greatest impact on the cost-effectiveness analysis. Figures 2 and 3 show that the largest variable in the oseltamivir therapy group and the favipiravir therapy group that had the greatest impact in this study was the cost of using Medical Consumables. The magnitude of the impact that arises due to the cost of using Medical Consumables requires special attention in order to maintain cost-effectiveness.

## Conclusion

The conclusion of this study is that the ACER value of COVID-19 patients using oseltamivir therapy is IDR 431,744 and the ACER value of COVID-19 patients using favipiravir therapy is IDR 367,010. The group of COVID-19 patients using favipiravir therapy is more cost-effective than the group of COVID-19 patients using oseltamivir therapy with an ICER value of IDR 60,605.30. These results can be used as a basis for allocating the drug procurement budget for COVID-19 patients, especially in situations of limited resources.

## Conflict of Interest

This research has no conflict of interest.

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