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Article review: Cost effectiveness analysis of antihypertensive amlodipine compared to captopril in health care facilities

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ABSTRACT

Hypertension, also known as high blood pressure, is a disease characterized by an increase in systolic blood pressure exceeding 140 mmHg and diastolic blood pressure exceeding 90 mmHg, in several measurements with a time of five minutes and with sufficient rest. The purpose of this study is to determine the cost effectiveness of hypertension therapy by using a comparison of amlodipine and captopril drug therapy in health service facilities. The method chosen was a literature study taken from journals and the results of previous research from various references related to the cost-effectiveness of antihypertensive therapy. Based on several journal literature or scientific publications that have been researched regarding the cost-effectiveness of amlodipine antihypertensive therapy compared to captopril, the results show that amlodipine has a higher effectiveness compared to captopril based on ACER and ICER values from several previous studies. Based on 10 literatures that have been analyzed, 7 literatures state that amlodipine antihypertensive is more Cost-Effective compared to captopril antihypertensive.

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1. Introduction

Hypertension is a condition in which systolic and diastolic blood pressure increases by more than 140 mmHg and more than 90 mmHg, with repeated measurements and in good condition. Hypertension is a disease that has a risk of cardiovascular complications (Hasan et al., 2023). Hypertension that occurs continuously and for a long time will cause store disease, heart attacks, heart failure, and chronic kidney failure. Many people with hypertension do not realize that they have hypertension so this disease is often referred to as a silent killer. This disease does not cause symptoms or signs before complications occur (Kuna et al., 2023).

The use of antihypertensive drugs can treat hypertension. Amlodipine is included in the Calcium Channel Blocker group and captopril is included in the Angiotensin Converting Enzym Inhibitor group) are two types of drugs commonly used to treat hypertension (Wirawan, 2020). The prevalence of hypertension sufferers in the world reaches around 1.13 billion people and is expected to increase in 2025 to 1.5 billion people and 9.4 million people die each year due to hypertension and its complications. Meanwhile, the prevalence of hypertension sufferers in Indonesia according to the 2018 Riskesdas has reached 34.11%. Health service financing has increased as evidenced by the 2018 budget allocation data

of 61.86 trillion rupiah with a budget usage of 57.35 trillion rupiah (Mokodompit et al., 2025). This data has increased from 2017 which only used a budget of 54.91 trillion rupiah. Cohort studies show that lowering blood pressure by around 5 to 10 mmHg can reduce the risk of death from type 2 diabetes by up to three times. The advantage of controlling blood pressure in hypertensive patients with type 2 diabetes compared to glycemic control is a significant reduction in the risk of microvascular complications (Amir & Kuna, 2024). Other benefits include improved quality of life and more efficient health care costs (Winta et al., 2018).

JNC VIII recommends low-dose thiazide diuretics or calcium channel blockers as initial treatment for hypertension and diabetes in black patients, but recommends low-dose thiazide diuretics as initial treatment for non-black patients, ACE inhibitors angiotensin receptor antagonists or calcium channel antagonists. The price of blood pressure-lowering drugs varies. Therefore, drug prices are an important factor in determining patient treatment choices. By considering these factors, pharmacoeconomics must be applied to support the use of antihypertensive drugs that are efficient, cost-effective, and pharmacologically effective (Mappa & Kuna, 2022). We rely on pharmacoeconomic analysis methods, including cost-effectiveness analysis. Cost-effectiveness analysis is an economic evaluation method used in decision making to choose the best option from several available options (Makalalag & Rasyid, 2024). The criteria for evaluating which option to choose is based on the total cost of each option, and the analyst or decision maker will choose the option with the lowest total value (Winta et al., 2018).

The effectiveness of treatment therapy often experiences problems in women after menopause because the cessation of endogenous estrogen production causes the body to be unable to maintain vasodilation that can control blood pressure. Hormones in men and women have the effect of regulating the RAS (Renin-Angiotensin System) and affecting angiotensinogen production and sodium metabolism. A decrease in estrogen hormone increases RAS regulation by increasing plasma renin activity. This is directly proportional to age in women and can be influenced by a person's physical activity. Likewise with comorbidities. Appropriate treatment reduces the incidence of death by 30% and can increase the incidence of death by 70%. In a study conducted by Nurhikmah (2019) entitled "Cost-Effectiveness Analysis of Oral Antihypertensive Drugs Amlodipine and Candesartan in Inpatient Hypertensive Patients at Pandan Aramboyolali Hospital in 2016", amlodipine was shown to have the best therapeutic effect. Amlodipine was shown to have the best therapeutic effect. to be a cost-effective antihypertensive agent. Dr. Anjani's research (2017) entitled "Cost-effectiveness analysis of antihypertensive drugs for hypertensive patients with complications of type 2 diabetes" and was presented at the Dr. Anjani International Conference. In 2017, Dr. Moewardi from Soetomo Hospital showed that the most effective and cost-effective antihypertensive drug was a combination of amlodipine 10 mg and captopril 25 mg. Based on this background, it is necessary to assess the cost-effectiveness of treatment to ensure that hypertensive patients receive the right treatment and prevent an increase in the prevalence of hypertension. Proper treatment will provide benefits to patients in terms of healing the disease, costs incurred, and compliance. This is especially true for patients who must take medication in the long term or for life, for example. High blood pressure.

2. Methods

The method chosen is a literature search from specialized journals and previous research results from various references regarding the cost-effectiveness of antihypertensive therapy. The purpose of this review is to provide an overview of relevant publications for better understanding. The criteria used are national and international scientific journals in the form of published manuscripts, and the number of studies used is 10 journals.

The research begins with a preparation stage. The preparation stage includes literature studies, problem formulation, proposal elaboration, and scientific paper searches. Search for scientific articles on Google Scholar, Pubmed, Portal Garuda, and Science Direct using the keywords efficacy, antihypertensive drugs, combination antihypertensive drugs, cost-benefit analysis of combination oral

antihypertensive drugs, or cost-benefit analysis of the use of combinations carried out Oral antihypertensive agents (Anjani, 2019).

The sample collection process by applying purposive sampling techniques based on predetermined criteria, including Indonesian language articles with relevant themes, and published in the last 5 years, namely articles published between 2019-2024. Articles with inaccessible full texts and articles found in the form of scientific papers, theses, dissertations, or review articles were not used in compiling this manuscript. The selected articles were then screened based on the established criteria. The screening results showed that there were 4 selected articles used as samples in compiling this manuscript. The selection process for articles used in this study was carried out using the PRISMA method (Bulan et al., 2022).

In this study, there are no specific criteria in selecting the literature used in the analysis, based on the research location, statistical methods, or research design, all are in accordance with the inclusion criteria that have been set and explained by the researcher. This study only uses 10 libraries as data sources because the data is sufficient to provide a strong conclusion about the cost-effectiveness of antihypertensive therapy in this case using the latest literature and accredited scientific articles so that its truth can be recognized

3. Results and Discussion

Table 1.
Cost-effectiveness of amlodipine compared to captopril based on ACER and ICER values

Drug Type	Effectiveness(%)	Value ACER	Value ICER
Amlodipin	62,23%	4233,3	1063,5
Captopril	57,14%	4904,0	-
Amlodipin	66,67%	79,90	-129,65
Captopril	85,77%	33,32	-
Amlodipin	86,7%	12.023,00	-
Captopril	60%	12.164,00	11.704,6
Amlodipin	-	32.931,28	-
Captopril	-	42.258,57	-
Amlodipin	58%	47.263,34	-
Captopril	100%	34.771,46	-
Amlodipin	63,2%	69,24	-
Captopril	61,5%	96,87	-
Amlodipin	78%	141.428,2	95.293,3
Captopril	63%	152.412,6	-
Amlodipin	86,7%	12.023,00	11.704,6
Captopril	60%	12.164,00	-
Amlodipin	43,75%	1.078	-
Captopril	50%	254	930
Amlodipin	-	1.353.707	-
Captopril	-	3.038.087	-

The purpose of cost-effectiveness analysis is to determine the relationship or comparison between health benefits and resources used in health programs so that policymakers can choose the best available treatment. The results of this analysis are expressed as a ratio, either the average cost-effectiveness ratio (ACER) or the incremental cost-effectiveness ratio (ICER).

ACER is used to represent the total cost of a medical intervention, which is then divided by the patient's clinical outcome. ACER is described as the number of rupees per specific clinical outcome achieved and is independent of the comparator. On the other hand, ICER is the ratio of the difference in cost between two available treatment options to the difference in effectiveness between those treatment options. The interpretation of ICER results is different from ACER results. The ICER value is used to indicate the cost required to improve the outcome by one unit relative to the comparator.

The treatment of hypertension aims to reduce mortality and morbidity associated with target organ damage, such as heart failure, coronary artery disease, and chronic kidney disease. Drug therapy involves the use of one or more antihypertensive drugs. When a single antihypertensive drug is unable to achieve the desired blood pressure control, a combination of drugs that have antihypertensive effects may be needed. Commonly known antihypertensive drugs include diuretics, ACE inhibitors, angiotensin receptor antagonists, calcium channel blockers, and beta-blockers (Nilansari et al., 2020).

The cost of treatment incurred by patients will vary depending on the type of treatment they choose. Treating hypertension is a relatively expensive and difficult long-term treatment. Therefore, a reference point is needed to assess the effectiveness of hypertension treatment for patients and its impact on their quality of life. Therefore, it can be used as a reference for planning better treatment, considering the cost and effectiveness of treatment for patients (Dianati et al., 2023).

According to Inform Kamri et al. (2021) in their study on "Cost-Effectiveness Analysis of the Use of Amlodipine and Captopril in Hypertensive Patients at Majene Hospital", the proportion of hypertensive patients who achieve treatment goals is higher than the proportion of hypertensive patients who achieve treatment goals. hypertensive patients who suffer from it Depends on the comorbidities they have. The efficacy was 69.23% when amlodipine 5 mg was used, and 57.14% when amlodipine 10 mg was used. The efficacy was 57.14% when using 12.5 mg of captopril, and 50% when using 25 mg of captopril. From the percentage obtained, it can be concluded that the effectiveness of therapy between amlodipine and captopril, both at low and high doses, shows that the group using amlodipine has better effectiveness compared to the group using captopril. These results are in line with previous studies showing that amlodipine is the first-choice antihypertensive with the best effectiveness, while captopril is in second place (Kristanti, 2015). In addition, other studies also confirm that amlodipine has a higher level of therapeutic effectiveness than captopril (Wirawan, 2020).

The results of statistical analysis using the Mann Whitney method showed that there was a statistically significant difference with p 005 in the average use of amlodipine and captopril at different doses. Although the cost of amlodipine is higher, interestingly, the amount of money spent on the use of other drugs is much higher for the use of captopril than amlodipine. The ACER value in the 5 mg amlodipine treatment group was lower than the ACER value in the 125 mg captopril treatment group. And the ACER value in the 10 mg amlodipine treatment group was also lower than the ACER value in the 25 mg captopril group. Therefore, based on this comparison, the low and high dose amlodipine treatment groups were more cost-effective than the captopril treatment group. ICER calculation should also be done if the cost of the intervention is higher but the effectiveness is higher. Therefore, the ICER value was calculated in the 5 mg amlodipine versus 125 mg captopril treatment groups. The ICER value is used to indicate additional costs and additional cost-effectiveness. If captopril treatment is used in hypertensive patients, then an additional cost of IDR 10,635 can increase the recovery of hypertensive patients in the amlodipine treatment group. The results of this study are similar to the study conducted by Wirawan in 2020 which looked at the cost-effectiveness analysis of hypertension treatment with amlodipine and captopril at Wirabuana Hospital, Palu, showing that amlodipine was more cost-effective than captopril .

Based on Bertolio's research (2020) on "Cost-effectiveness analysis of single-use antihypertensive drugs for hypertensive patients at the Danurejan District Health Center", hydrochlorothiazide has the highest antihypertensive effect, which is 88.89%. The target blood pressure was achieved in nine patients. After that, the use of the antihypertensive drug captopril achieved the target blood pressure in 6 patients by 85.77%, followed by the use of amlodipine by 66.67%, two patients effectively achieved the target blood pressure, and patients receiving furosemide achieved the target blood pressure by 50%, 1 patient achieved the target blood pressure based on patient calculations. This is because it is the most cost-effective option for patients using captopril and can produce better clinical outcomes with lower health care costs (Alifiar et al., 2018).

Next are patients using hydrochlorothiazide, followed by those using furosemide, and finally those using amlodipine. We assume that the patient buys one antihypertensive drug and considers the cost of antihypertensive drugs, which is the price of each individual antihypertensive drug that is not

included in the cost per unit of treatment. From the perspective of the cost of antihypertensive drugs (base drug price), the use of hydrochlorothiazide is the most cost-effective. Hydrochlorothiazide results in a significant reduction in morbidity (stroke and myocardial infarction) and mortality. In addition, thiazide diuretics are cheaper than other drugs, so they are more often chosen (Nilansari et al., 2020). Followed by captopril, furosemide, and finally amlodipine. If the patient uses hydrochlorothiazide therapy, an additional cost will be incurred to increase the effectiveness of captopril of IDR 81.41.

According to Bulan et al. (2022) Study "Cost-effectiveness analysis of captopril and amlodipine in hypertension with diabetes" The cost-effectiveness study "Meritas at the Magelang Regency Health Center" showed that a single dose of 10 mg amlodipine has been proven effective. proven to be the main treatment option. The determination of the cost-effectiveness column in both treatment groups also shows that the ICER calculation is not necessary. However, if you want to know more about the effectiveness of your treatment regimen, you can calculate the ICER value (Tantri, 2020). The smaller or more negative the ICER value, the more effective the treatment option is and can be used as the best treatment recommendation (Abdulah et al., 2017).

The ICER value shows the additional cost of switching treatment from combination antihypertensive therapy to monotherapy. The provision of this treatment resulted in a negative ICER value of (-) IDR 223,246.40. On this basis, a single dose of 10 mg amlodipine appears to be a more cost-effective agent in the treatment of hypertensive patients with type II diabetes.

Based on Wirawan's research (2020) entitled "Cost Effectiveness Analysis of Hypertension Treatment with a Comparison of Amlodipine and Captopril Pharmacotherapy at Wirawan Hospital, Palu", the results of the ACER value calculation showed the ACER value of Captopril of IDR 42,258.57. The ACER value for amlodipine is Rp32,931.28. From these results, it can be concluded that the ACER value of amlodipine is lower than the ACER value of captopril, therefore amlodipine is more cost-effective than captopril (Arief & George, 2020). Amlodipine is the drug of choice for treating high blood pressure. This drug is an antihypertensive CCB whose mechanism of action is to prevent calcium penetration into cells, causing vasodilation, slowing the heart rate, and reducing myocardial contractility. This lowers blood pressure (Arief & George, 2020). This CCB is the most widely used antihypertensive drug compared to other groups of antihypertensive drugs, especially amlodipine (Baharuddin, 2013).

In addition, based on the average price, the price difference between the two drugs above is also very far, where the price of Captopril is more expensive than the price of Amlodipine, which is Rp35,939.00. Therefore, based on this study, it is recommended to choose amlodipine for the treatment of hypertension because it is cost-effective and relatively inexpensive (Baharuddin, 2013). Anjani (2019) at Dr. Soetomo Hospital. "Mowardi 2017" Amlodipine 10mg and Captopril 25mg were concluded as the most cost-effective antihypertensive drugs for hypertensive patients, because they had the lowest ACER of IDR 13,605.06, even though there were changes in the direct medical cost components. You can. Doctors with complications of type 2 diabetes. Soetomo General Hospital. In Moewadi in 2017, a combination of amlodipine 10 mg and captopril 25 mg was used.

According to (Normansyah, 2020) in a study entitled "Comparison of Cost Effectiveness of Amlodipine and Captopril Treatment in Outpatient Hypertension Patients at the Joharbal District Health Center in 2018", the cost effectiveness of drugs is based on the ACER value, which is the average cost of treatment per patient divided by the effect of treatment. In this study, 63.2% of amlodipine patients and 61.5% of captopril patients achieved treatment goals. The average cost of treatment with amlodipine was IDR 4,376.00 and the average cost of treatment with captopril was IDR 5,958.00. An independent t-test on the average treatment costs produced a P value of 0.00, indicating a significant difference between the average treatment costs of amlodipine and captopril. The ACER result for amlodipine was 69.24 cents/1% effectiveness, while the ACER result for captopril was 96.87 cents/1% effectiveness. Based on the ACER value, it can be concluded that amlodipine is more cost-effective than captopril.

Based on study (Tabita, 2022) entitled "Cost-Effectiveness Analysis of Amlodipine and Captopril Therapy in Outpatient Hypertension Patients at the Red and White Clinic in Hungary, November 2022 Period", the cost-effectiveness is calculated as follows: form: represented. ACER (average cost-

effectiveness ratio) is determined by comparing the average monthly costs (costs) of various treatment patterns with the effectiveness (outcome or effectiveness) of the treatment pattern in achieving the expected blood pressure Amlodipine 5 mg with an ACER value of Rp is the most cost-effective antihypertensive treatment pattern.143,300 (Andayani, 2020) following applies to ACER: the lower the ACER value, the more cost-effective the drug is. Therefore, for a 1% increase in drug efficacy when using 16 mg candesartan, the cost will be equivalent to the ACER value, or Rp23,489. ICER is defined as the ratio or difference in cost between two alternatives and the difference in effectiveness between the same two alternatives (Andayani, 2020).

The comparison group in treatment regimens A and C had the highest ICER value (IDR 205,500), while the comparison group in treatment regimens A and D had the lowest ICER value (IDR 30,000). 131,300, and comparing treatment plans A and B, the ICER value is lower, which is IDR 25,050 (Andayani, 2013). Based on a study conducted by (Bulan et al., 2022) entitled "Cost Effectiveness Analysis of Captopril and Amlodipine Drugs in Hypertensive Diabetic Patients at the Magelang Provincial Health Center", the effectiveness rate of 10 mg amlodipine therapy was 86.7% (Bulan, 2020). This has been known. On the other hand, the rate with 25 mg captopril is 60%. The average direct medical cost in the amlodipine 10 mg/day group was IDR10,423.93, higher than the average direct medical cost in the captopril 25 mg/day group, which was IDR7,298.80. The ACER value for amlodipine 10 mg per day was IDR12,023.00, and for captopril 25 mg per day was IDR12,164.00 (Tyas et al., 2021).

The ICER value was calculated at IDR11,704.6. According to (Hadning et al., 2019) in a study entitled "Cost-effectiveness analysis of the use of captopril and amlodipine in outpatients with primary hypertension at the Sagan Health Center", the efficacy rate of amlodipine 10 mg/day was 86.7%. In contrast, the efficacy rate of captopril at 25 mg/day was 86.7%. Increased by 60%. The average direct medical cost for amlodipine 10 mg per day was Rp10,429.30 higher compared to Rp7,298.80 for captopril 25 mg per day. The ACER value for amlodipine 10 mg per day was Rp12,023.00 and the ACER value for captopril 25 mg per day was Rp12,164.00. The mean ICER value for calculating direct medical costs in the amlodipine 10 mg/day group was Rp10,423.93 higher than the captopril 25 mg/day group of Rp7,298.80. Conclusion: Amlodipine is more cost-effective than captopril with an ACER value of Rp12,023.00. According to in a study on "Cost-effectiveness analysis of hypertension treatment with captopril in patients treated at Pandan Alamboyorali Hospital in 2017", amlodipine is the most cost-effective treatment group in terms of ACER value of Rp. 1,353,707, while captopril has a higher ACER value of Rp. 3,038,087 (Irganda, 2021).

4. Conclusion

Based on several journal literature or scientific publications that have been studied related to the cost-effectiveness of antihypertensive drug therapy amlodipine and captopril, amlodipine has a higher effectiveness compared to captopril based on the ACER and ICER values from several previous studies. Based on 10 literatures that have been analyzed, 7 literatures state that antihypertensive amlodipine is more Cost-Effectiveness compared to antihypertensive captopril. There has been no decision-making because this needs to be discussed by stakeholders in health care facilities. However, there have been several doctors who have prescribed the drug to patients.

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