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REVIEW: COST EFFECTIVENESS ANALYSIS AND ITS IMPLEMENTATION REGARDING HYPERTENSION TREATMENT

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ABSTRACT

Healthcare financing involves the management of various efforts to mobilize, allocate, and spend health funds to ensure the implementation of health development aimed at achieving the highest possible level of public health. Hypertension, a non-communicable disease (NCD) continues to evolve and poses a serious public health issue and leads to an increasing health financing burden. Health Social Security Agency (BPJS) indicated direct medical costs of hypertension IDR 3 trillion in 2017 and 2018. The variety of first-line antihypertensive combinations due to the numerous recommended first-line antihypertensive combinations in various guidelines highlights the importance of pharmacoeconomic studies to determine the most cost-effective combination. This review article aims to further discuss the implementation of the CEA method as a basis for treatment selection or decision-making regarding hypertension treatment. The nifedipine 60 mg and candesartan 32 mg combination is deemed the best, achieving a blood pressure reduction of 23,8/16,5 mmHg (p<0,01) compared to placebo and monotherapy reductions of 5,3/6,7 mmHg. Additionally, the nifedipine GITS - candesartan combination reduces vasodilator side effects incidence to 18,3% compared to 23,6% for nifedipine monotherapy, including a lower incidence of headaches (5,5% vs. 11%)..

KEYWORDS *Hypertension, Cost-Effectiveness Analysis (CEA), Angiotensin Receptor Blocker (ARB), Calcium Channel Blocker (CCB).*

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INTRODUCTION

Healthcare financing involves the management of various efforts to mobilize, allocate, and spend health funds to ensure the implementation of health development aimed at achieving the highest possible level of public health (Kemenkes RI, 2022). The total healthcare expenditure since 2013 to 2020 has consistently increased, almost doubling. From IDR 260,7 trillion in 2012 to IDR 561,8 trillion in 2020 (Kemenkes RI, 2022). This trend suggests that healthcare costs will continue to rise, necessitating studies on improving the efficiency and effectiveness of healthcare spending. An economic health review is essential for better healthcare decision-making (Albright, 2024).

Hypertension, a non-communicable disease (NCD) with a global prevalence of 26.4%, continues to evolve and poses a serious public health issue linked to life-threatening cardiovascular diseases (Casmuti & Fibriana, 2023; Liu et al., 2021). In 2019, cardiovascular-related Elevated Systolic Blood Pressure (ESBP) accounted for 2,717,475 Years Lived with Disability (YLD). Hypertension must be effectively managed and controlled to prevent severe disabilities or death and avoid prolonged and costly treatments. In the United States, the average annual direct medical costs due to hypertension were estimated at $47,3 billion for 2012 - 2013, while in Indonesia, data from the Health Social Security Agency (BPJS) indicated direct medical costs of IDR 3 trillion in 2017 and 2018 (Kemenkes RI, 2019; Park et al., 2017).

The costs of hypertension treatment vary due to the numerous recommended first-line antihypertensive combinations in various guidelines. The Joint National Committee's Eighth Report (JNC 8) and the Indonesian Society of Hypertension recommend first-line antihypertensive combinations of ACEI or ARB with CCB or diuretics (Esh et al., 2018; Indonesian Society Of Hipertension, 2019). The variety of first-line antihypertensive combinations highlights the importance of pharmacoeconomic studies to determine the most cost-effective combination.

Pharmacoeconomics is a branch of health economics that focuses specifically on the costs and benefits of particular interventions compared to existing ones (comparator) (Tonin et al., 2021). Understanding pharmacoeconomic is crucial for clinical pharmacologists promoting rational prescribing or conducting clinical trials that include economic components. Pharmacoeconomics also aids decision-makers (such as healthcare professionals and stakeholders) as well as health service providers in assessing whether a health intervention provides more affordable and efficient economic value with limited resources. The fundamental concept of health economic evaluation is comparative, involving the comparison of two or more interventions, programs, strategies, or policies regarding the resources allocated and the outcomes produced (Keifer & Effenberger, 2022). The most commonly used pharmacoeconomic study method for analyzing the cost-effectiveness of hypertension combinations is Cost-Effectiveness Analysis (CEA), which compares costs in monetary units (e.g., Rupiah) to health outcomes in clinical effectiveness (Alzarea et al., 2022).

This review article aims to further discuss the implementation of the CEA method as a basis for treatment selection or decision-making regarding hypertension treatment.

RESEARCH METHOD

Tools and Materials

The preparation of this review article uses the literature study method with primary data sources in the form of articles and research journals that have been published and can be downloaded online via national and international journal websites such as Google Scholar, ScienceDirect, PubMed, and Garuda. The citation process in this article review uses the Mendeley® tool

Article Selection Criteria

The journals selected in the process of preparing this review article are those that certain inclusion and exclusion criteria. The inclusion criteria determined in selecting journals were journals containing information about hypertension and analysis of its cost effectiveness that were published no later than 10 years from the process of preparing this review article. While the exclusion criteria are journals published before 2014.

Research Procedure

The steps of preparing this article review began with collection for journals regard hypertension treatment and its medical cost during the treatment process. Then the author evaluates the main points in the article and journal, then summarizes and presents them in this article review.

RESULT AND DISCUSSION

Cost Effectiveness Analysis (CEA) is the most widely used economic evaluation method as it can compare at least two health interventions in monetary units against quantitative health units, such as the number of cases treated, blood pressure reduction in mmHg, or life years gained (Indrayathi, 2021; Tonin et al., 2021). This method involves problem identification, identification of available and competing treatment interventions, identification of the consequences and trade-offs of treatment interventions, evaluation of evidence (such as costs and incidence rates), finding simplified ways to measure health, and determining the value of each intervention (Albright, 2024).

CEA is not always necessary for doctors, practitioners, or decision-makers to determine the best treatment intervention. Analysis is only required when an intervention has higher costs but unknown and/or better outcomes in a specific clinical scenario (Albright, 2024). Furthermore, the use of CEA can be guided by a cost-effectiveness plane diagram. If the intervention falls in quadrants I and III, CEA needs to be conducted through Incremental Cost Effectiveness Ratio (ICER) calculation by comparing the incremental cost to the incremental effect of the intervention and the comparator (Tonin et al., 2021). The ICER results then determine whether the intervention will be accepted, depending on the willingness-to-pay threshold (Fernandez, 2023).

As an economic evaluation method, the perspective on evaluating costs is fundamental in CEA calculations, as it determines the cost components to be

considered (Brandão et al., 2023). The societal perspective is recommended as it includes all costs, both direct and indirect (Brandão et al., 2023).

There are two types of CEA: short-term analysis and long-term analysis. Short-term analysis, conducted for less than one year, is the most frequently performed, with unit costs calculated from depreciation costs. In contrast, long-term analysis, conducted for over one year, uses discounted unit costs without considering depreciation costs (Indrayathi, 2021). Long-term CEA requires adjusting cost and benefit data that occur at different times or in different countries and currencies (Brandão et al., 2023).

Hypertension is currently the third largest disease worldwide, prompting continuous research, including the costs of its treatment. A study at Panti Waluya Hospital in Malang compared the effectiveness of amlodipine and nifedipine in lowering systolic and diastolic blood pressure from the hospital's perspective. The ACER calculation showed that amlodipine had lower costs compared to nifedipine, but nifedipine was more effective in achieving blood pressure targets of <140/90 mmHg, making nifedipine more cost-effective (Wicaksono et al., 2023).

Another study at RSI NU Demak on BPJS outpatients with hypertension and diabetes mellitus (DM) comorbidity analyzed the cost-effectiveness of ARB - CCB versus CCB - ACEI combinations. The ACER calculation indicated that the CCB - ACEI combination was more cost-effective, while the ICER calculation favored the ARB - CCB combination with a value of IDR 58,401.38 (Heroweti & Rokhmawati, 2023).

Research also reveals that the ACEI - CCB combination is optimal in preventing cardiovascular events, but the benefits of ACEI - CCB compared to ARB remain uncertain. The DISTINCT (reDefining Intervention with Studies Testing Innovative Nifedipine GITS – Candesartan Therapy) study was conducted to evaluate the dose response and tolerability of nifedipine GITS and/or candesartan (Kjeldsen et al., 2014). The study found that the nifedipine GITS and candesartan combination significantly reduced blood pressure both SBP and DBP compared to placebo and monotherapy, at week 8 of use ($p<0.05$) (Kjeldsen et al., 2014). The greatest reduction in blood pressure resulted from a combination of 60 mg nifedipine and 32 mg candesartan which reached -23,8/- 16,5 mmHg ($p<0.01$) when compared to placebo and monotherapy respectively which only decreased 5,3/ 6,7 mmHg (Kjeldsen et al., 2014). The nifedipine – candesartan combination also showed a lower incidence of vasodilator side effects of 18,3% when compared with nifedipine monotherapy (23,6%) and included the incidence of headaches (5,5% versus 11%) (Kjeldsen et al., 2014).

CEA method was also used to assess the effectiveness of the International Society of Hypertension 2020 Guideline in Ethiopia from a societal perspective. The guideline implementation could prevent 22.348,66 productive years lost annually, with additional monetary benefits totaling $128.520.077,66 and a willingness-to-pay threshold of $50.000 per DALY avoided (Davari et al., 2022).

Table I. Definition of Main Components of Economic Evaluation

Component	Definition
Target population	A group or subgroup that will get benefits from the health intervention
Comparison	An interventions are compared in an economic evaluation
Perspective	Points of view in assessing health benefits and costs (e.g., patients, health care providers, payers, societal large)
Possible costs	Represents the lost benefits that would have been gained if an option or intervention had not been selected
Cost	Refers to the monetary component of economic analysis. Costs can be divided to direct medical and non-medical costs, indirect costs, and intangible costs
Results	Also called the expected health or humanistic 'benefits' or 'consequences' or 'outcomes' of an intervention
Willingness to Pay (WTP)	The process by which individuals are asked the maximum amount they are willing to pay (in monetary terms) to achieve a particular benefit from an intervention/service

(Sumber : Tonin et al., 2021)

Table II. Classification of Cost dan Perspective

Fee Type		Cost component	Perspective			
			Society	Patient	Health Care Providers	Payer
Direct cost	Medical	Drug costs	+	+	+	+
		Doctor Consultation Fees	+	+	+	+
		Cost of supporting examinations (laboratory tests)	+	+	+	+
		Cost of health care workers	+	+	+	+
		Administrative costs	+	+	+	+
		Other additional costs	-	+	-	-
	Non-medical	Travel expense	+	+	-	-
		Meal cost	+	+	-	-
Indirect costs		Morbidity Costs	+	+	-	-
		Mortality Costs	+	+	-	-
Intangible costs		Pain, sadness/sorrow, and/or suffering	+	+	-	-

(Sumber : Fadhilah & Sari, 2019; Mulianingsih et al., 2021)

CONCLUSION

Cost-Effectiveness Analysis is the most commonly used method for analyzing hypertension treatment effectiveness. The nifedipine 60 mg and candesartan 32 mg combination is deemed the best, achieving a blood pressure reduction of 23,8/16,5 mmHg (p<0,01) compared to placebo and monotherapy reductions of 5,3/6,7 mmHg. Additionally, the nifedipine GITS - candesartan combination reduces vasodilator side effects incidence to 18,3% compared to 23,6% for nifedipine monotherapy, including a lower incidence of headaches (5,5% vs. 11%).

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