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Cost-effectiveness analysis of metformin-glimepiride vs metformin-vildagliptin on glycemic control in type 2 diabetes patients at RSUD dr. Soekardjo

Wahyu Permana[1*], Nur Rahayuningsih[1], Rahmawati[1]

[1]*Department of Pharmacy, Faculty of Pharmacy, Universitas Bakti Tunas Husada, Tasikmalaya, 46115, Indonesia.*

*Corresponding Author: nurrahayuningsih@universitas-bth.ac.id

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ABSTRACT: Type 2 Diabetes Mellitus is a major public health problem that substantially contributes to the long-term healthcare cost burden. Combination therapy is often required to achieve optimal glycemic control; however, economic considerations are important in selecting an appropriate therapeutic regimen. This study aimed to analyze the cost-effectiveness of metformin–glimepiride (M-G) compared with metformin-vildagliptin (M-V) combination therapy in achieving glycemic control among outpatients with T2DM at a regional public hospital in Indonesia. A retrospective observational study with a cost-effectiveness analysis approach was conducted from January to April 2026 using medical record data from 2025. A total of 32 eligible patients were enrolled in the study, including 24 patients who received the M-G regimen and 8 patients who received the M-V regimen. Direct medical costs were estimated from the provider perspective using hospital medical and financial records and included costs associated with medications, physician consultations, laboratory examinations, and hospital services.Effectiveness was measured based on the percentage reduction in random plasma glucose levels. The results showed that the M-V combination demonstrated higher effectiveness (62.5%) compared with M-G (50%), with a difference of 12.5%. However, the average direct medical cost in the M-V group was higher (IDR 370.659) than in the M-G group (IDR 244,589). The average cost-effectiveness ratio (ACER) was lower in the M-G group (IDR 4,891.78) compared with the M-V group (IDR 5,930.54). The incremental cost-effectiveness ratio (ICER) indicated that each additional 1% increase in effectiveness with M-V required an additional cost of IDR 10,085.60. Therefore, based on effectiveness outcomes, the M-V combination was considered more cost-effective.

KEYWORDS: Cost-effectiveness analysis; direct medical costs; glycemic control; metformin combination; T2DM.

INTRODUCTION

Type 2 Diabetes Mellitus (T2DM) is the most common form of diabetes, characterized by insulin resistance and impaired insulin secretion by pancreatic beta cells. This condition leads to chronic hyperglycemia and may result in long-term complications if not properly managed [1]. The rising incidence of T2DM globally and nationally correlates with numerous risk factors, such as lifestyle modifications, heightened intake of calorically dense and fatty foods, sedentary behaviour, obesity, demographic ageing, and genetic susceptibility [2], [3].

According to the International Diabetes Federation (IDF) Diabetes Atlas 2025, diabetes is a global health challenge with 588.7 million people aged 20-79 living with the disease in 2024, and this number is predicted to increase to 852.5 million by 2050. Indonesia ranks fifth in the world with 19.2 million people living with diabetes in 2024, projected to reach 28.6 million by 2050 [4]. Based on the 2023 Riskesdas, the prevalence of DM in Indonesia reached 10.7% (19.5 million people), in West Java, the prevalence was 1.74% or around 570,611 sufferers [2]. Based on data from the West Java Provincial Health Office in 2023, out of 757,815 residents of Tasikmalaya City, there were 11,782 people with diabetes [5], [6].

The primary goal of T2DM management is to achieve optimal glycemic control in order to prevent chronic complications. Metformin is generally recommended as the first-line therapy, however combination therapy is required in most patients to achieve better glycemic targets [1]. Agents that can be combined with metformin as second-line therapy include sulfonylureas, such as glimepiride, and dipeptidyl peptidase-4

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(DPP-4) inhibitors, such as vildagliptin [7]. Sulfonylureas are commonly combined with metformin because their complementary mechanisms of action improve glycemic control by simultaneously enhancing insulin sensitivity and stimulating endogenous insulin secretion. This combination has demonstrated high glycemic efficacy and remains widely used as a second-line treatment owing to its relatively low acquisition cost and broad availability, particularly in low- and middle-income countries [8]. In contrast, dipeptidyl peptidase-4 (DPP-4) inhibitors are also recommended as second-line agents in combination with metformin because they improve glycemic control through glucose-dependent stimulation of insulin secretion and suppression of glucagon release. Compared with sulfonylureas, DPP-4 inhibitors have a higher acquisition cost but are associated with a lower risk of hypoglycemia and are generally weight-neutral, making them a suitable therapeutic option for older adults and patients at increased risk of hypoglycemia [1], [9].

Alongside its growing prevalence, type 2 diabetes mellitus (T2DM) imposes a substantial economic burden on Indonesia's healthcare system because of the need for lifelong treatment, regular monitoring, and the management of diabetes-related complications. Under Indonesia's National Health Insurance (Jaminan Kesehatan Nasional, JKN), diabetes is among the major chronic diseases contributing to healthcare expenditure, with financing continuing to increase annually due to long-term treatment and complication management. Therefore, the application of pharmacoeconomic analysis is essential in determining the most efficient and cost-effective therapeutic options [10],[11].

Pharmacoeconomics is a discipline that evaluates the relationship between costs and clinical outcomes of a therapeutic intervention in order to support decision makers in selecting the most efficient treatment alternatives [12]. *Cost-Effectiveness Analysis* (CEA) is a widely adopted pharmacoeconomic evaluation method for comparing the costs and clinical outcomes of alternative healthcare interventions. In CEA, effectiveness is measured using natural clinical outcomes, such as blood glucose levels, life-years gained, or the number of cases prevented, while costs are evaluated in monetary terms. By examining both the costs and health outcomes of competing interventions, CEA provides evidence to support healthcare decision-making regarding the relative value of alternative treatment strategies. However, conclusions about cost-effectiveness should be based on incremental comparisons and interpreted in accordance with appropriate decision-making criteria [13].

Previous pharmacoeconomic studies have demonstrated that sulfonylurea-based regimens are generally associated with lower treatment costs and favorable cost-effectiveness because of their relatively low acquisition costs. In contrast, DPP-4 inhibitor-based regimens offer several clinical benefits, including a lower risk of hypoglycemia and a weight-neutral profile, although these advantages are accompanied by higher acquisition costs [9], [10]. In Indonesia, several cost-effectiveness studies have investigated metformin, glimepiride, and other oral antidiabetic therapies in both hospital and primary healthcare settings. However, these studies primarily compared monotherapy with combination therapy or evaluated metformin–glimepiride against other treatment alternatives, rather than directly comparing metformin–glimepiride with metformin–vildagliptin combination therapy [14], [15], [16]. Moreover, most previous investigations focused on individual treatment regimens and did not specifically examine the economic trade-off between a lower-cost sulfonylurea-based combination and a higher-cost DPP-4 inhibitor-based combination using real-world hospital data from the Indonesian healthcare setting. Consequently, evidence regarding the comparative cost-effectiveness of metformin–glimepiride and metformin–vildagliptin from the hospital provider perspective remains limited. Therefore, the present study was undertaken to address this evidence gap by comparing the direct medical costs and clinical effectiveness of these two treatment regimens among patients with T2DM treated at RSUD Dr. Soekardjo.

▪ MATERIALS AND METHODS

This research utilised a Cost-Effectiveness Analysis (CEA) methodology. This study received ethical approval from the Health Research Ethics Committee of Universitas Bakti Tunas Husada Tasikmalaya (Approval No. 047-01/E.01/KEPK-BTH/II/2026). This retrospective observational study was conducted at RSUD Dr. Soekardjo Tasikmalaya. Medical records of outpatients with type 2 diabetes mellitus who received metformin–glimepiride or metformin–vildagliptin combination therapy between January and December 2025 were retrospectively reviewed. Data collection and analysis were carried out from January to April 2026. The cost-effectiveness analysis was performed using a one-month time horizon for each patient. Direct medical costs, comprising medication, physician consultation, laboratory examination, and hospital service

costs, were assessed alongside treatment effectiveness, which was determined based on random blood glucose (RBG) control during the same one-month observation period.

The study population comprised outpatients diagnosed with T2DM between January and December 2025 who were administered either M-G or M-V combination therapy. Patients were selected through purposive sampling from the medical records of outpatients with type 2 diabetes mellitus who received either M-G or M-V combination therapy between January and December 2025. Eligible patients were identified according to predefined inclusion and exclusion criteria, and all qualifying cases were included in the study, resulting in a final sample of 32 patients (24 in the M-G and 8 in the M-V).

The inclusion criteria were outpatients diagnosed with type 2 diabetes mellitus (T2DM) at RSUD Dr. Soekardjo who received metformin–glimepiride or metformin–vildagliptin combination therapy between January and December 2025, had complete medical records, and had or did not have diabetes-related comorbidities. Baseline random blood glucose (RBG) was defined as the measurement recorded before initiation of combination therapy, while follow-up RBG was the measurement recorded after one month of treatment. The change in RBG was calculated by comparing these two measurements, and both treatment groups were evaluated using the same one-month assessment interval. Comorbidity profiles were summarized descriptively and compared between treatment groups as baseline characteristics; however, no statistical adjustment for comorbidities was performed because of the limited sample size. The exclusion criteria included patients who discontinued therapy during the study period, including those who were referred to another healthcare facility or who died.

Data were obtained from patients' medical records and included demographic characteristics, laboratory results, and medication profiles. The economic evaluation was conducted from the hospital provider perspective. Direct medical costs were obtained from hospital medical and billing records and included expenditures for medications, physician consultations, laboratory examinations, and hospital services. Cost estimation was performed at the individual patient level by aggregating all direct medical costs incurred over the one-month treatment period. Unit cost data were based on the hospital tariff schedule recorded in the billing system. No indirect or non-medical costs were considered in the analysis. . Data were analyzed using Cost-Effectiveness Analysis (CEA) by calculating the Average Cost-Effectiveness Ratio (ACER) and the Incremental Cost-Effectiveness Ratio (ICER).

$$ACER = \frac{Cost}{Effectiveness}$$

$$ICER = \frac{\Delta Cost}{\Delta Effectiveness}$$

Descriptive statistics were used to summarize baseline characteristics, direct medical costs, and treatment effectiveness. Continuous variables were presented as means, whereas categorical variables were expressed as frequencies and percentages. The difference in treatment effectiveness between the two groups was evaluated using Fisher's exact test because of the small sample size. A two-sided p-value of <0.05 was considered statistically significant.

▪ RESULTS AND DISCUSSION

Table 1. Demographic characteristics of patients.

		M-G (n=24)	M-V (n=8)	∑ (n=32)	%
Gender	Female	16	6	22	68.75
	Male	8	2	10	31.25
Age	17-25	-	-	-	-
	26-35	2	1	3	9.38
	36-45	1	-	1	3.13
	46-55	3	1	4	12.50
	56-65	14	2	16	50
	>65	4	4	8	25
Educational Level	Primary education	11	3	14	43.75

		M-G (n=24)	M-V (n=8)	∑ (n=32)	%
Occupation	Junior high school	1	1	2	6.25
	Senior high school	6	3	9	28.13
	D-III	2	1	3	9.38
	No formal education	4	-	4	12.50
	Houswife	9	6	15	46.88
	Self-employed	3	1	4	12.5
	Civil servant	4	-	4	12.5
	Retaired	2	1	3	9.38
	Laborer	3	-	3	9.38
	Other	3	-	3	9.38
Payment Status	BPJS	24	8	32	100
Comorbidities	DM only	8	5	13	40.63
	DM, Hyperuricemia	2	-	2	6.25
	DM, Hypertension	13	1	14	43.75
	DM,Heart disease	1	2	3	9.38

Table 1 shows that patients with T2DM at RSUD Dr. Soekardjo Tasikmalaya, were predominantly female. This finding may be associated with hormonal changes and a decline in estrogen levels. Estrogen is recognised for its beneficial influence on insulin sensitivity and the distribution of body fat. Consequently, its loss may lead to heightened insulin resistance and visceral fat buildup, both of which are significant factors in the development of T2DM. Besides hormonal influences, disparities in body composition between males and females may also play a role in metabolic risk variances. Women tend to experience an increase in total body fat and alterations in fat distribution after menopause, which are associated with a higher risk of metabolic syndrome and impaired glucose tolerance [3], [17].

The majority of patients were in the 56–65 years and >65 years age groups, consistent with the epidemiological pattern of T2DM, which demonstrates an increasing prevalence with advancing age. The aging process is associated with insulin resistance, metabolic dysfunction, and a higher burden of comorbidities, all of which contribute to greater clinical management complexity. Furthermore, findings from the Longitudinal Ageing Study in India indicate an increasing prevalence of diabetes and its associated risk factors among older adults. These trends are influenced by urbanization, lifestyle transitions, and socioeconomic factors affecting the elderly population [18], [19].

The majority of patients in this study had a primary education level (40.63%), indicating the predominance of individuals with low educational attainment. Education is a social determinant that influences both the incidence and management of T2DM. Recent studies have demonstrated that lower educational levels are associated with a higher prevalence of T2DM and poorer glycemic control, which may be attributed to limited health literacy [20]. In addition, lower educational attainment is frequently associated with lower socioeconomic status and limited access to preventive healthcare services, which may indirectly influence treatment success and overall clinical outcomes [4].

The predominance of respondents who were housewives in this study has epidemiological implications, as low levels of occupational and daily physical activity are associated with an increased risk of T2DM. Cohort studies have demonstrated that reduced workplace physical activity is significantly associated with a higher incidence of T2DM, particularly among individuals with obesity. Moreover, low levels of physical activity have consistently been linked to a greater risk of diabetes compared with moderate to high levels of physical activity [21], [22].

Table 1 indicates that the most prevalent comorbidity among patients with T2DM was hypertension (43.75%), followed by T2DM without additional comorbidities (40.63%), T2DM with heart disease (9.38%), and T2DM with hyperuricemia (6.25%). Hypertension was the most common comorbidity in this study, accounting for 54.2% of patients in the M-G regimen and 12.5% in the M-V regimen. This finding is consistent with previous studies reporting that hypertension is the most prevalent comorbidity among patients with T2DM because both conditions share common pathophysiological mechanisms, including insulin resistance and endothelial dysfunction, and their coexistence substantially increases cardiovascular

risk. Furthermore, patients with diabetes and hypertension generally require additional antihypertensive medications, laboratory monitoring, and physician consultations, which may increase healthcare utilization and direct medical costs. Therefore, differences in hypertension prevalence between treatment groups should be considered when interpreting the comparative cost-effectiveness of the two treatment regimens [23]. The high prevalence of this coexistence reflects the underlying pathophysiological link between T2DM and hypertension, indicating that hypertension is the most frequently associated comorbidity across diverse clinical populations [24]. Hypertension and Type 2 Diabetes Mellitus (T2DM) exhibit shared risk factors, such as advanced age, obesity, and physical inactivity, which combine exacerbate the cardiometabolic profile of patients and elevate the risk of cardiovascular consequences [25].

In addition to hypertension, cardiovascular comorbidities, particularly heart disease, were identified in 9.38% of the study population and were more prevalent among patients receiving metformin–vildagliptin than among those receiving metformin–glimepiride (25.0% vs. 4.2%). This observation is consistent with the established pathophysiological link between type 2 diabetes mellitus (T2DM) and cardiovascular disease, whereby chronic hyperglycemia promotes endothelial dysfunction, oxidative stress, systemic inflammation, and accelerated atherosclerosis, thereby increasing the risk of coronary artery disease and heart failure [26]. Cardiovascular disease remains a major contributor to morbidity and mortality in individuals with T2DM and imposes a substantial burden on healthcare systems through increased utilization of long-term pharmacotherapy, specialist care, laboratory monitoring, and the management of cardiovascular complications he greater proportion of patients with cardiovascular disease in the metformin–vildagliptin group may reflect routine clinical prescribing practices, as DPP-4 inhibitors are associated with a lower risk of hypoglycemia than sulfonylureas and are therefore often considered more appropriate for older adults or patients with multiple comorbidities who require individualized therapeutic approaches [27].

Hyperuricemia was identified in 6.25% of the study population and was observed exclusively in the M-G regimen (8.3%), with no cases reported among patients receiving M-V. Hyperuricemia is a common metabolic abnormality in individuals with T2DM and has been associated with insulin resistance, dyslipidemia, and impaired renal function, all of which may contribute to an increased risk of adverse cardiometabolic outcomes [28]. Previous studies have further demonstrated that elevated serum uric acid levels are associated with suboptimal glycemic control and an increased risk of diabetes-related complications, suggesting that hyperuricemia may adversely influence disease progression and long-term clinical outcomes [29].

Table 2. Average direct medical cost per patient per visit.

Cost component	M-G (n=24)	M-V (n=8)
Medication cost	IDR 88,440.96	IDR 149,722.25
Physician consultation	IDR 108,166.67	IDR 140,000.00
Laboratory examination	IDR 44,487.50	IDR 77,437.50
Hospital service costs	IDR 3,500.00	IDR 3,500.00
Total direct medical cost	**IDR 244,589**	**IDR 370,659**

Based on Table 2, the M-G combination was the most frequently prescribed therapy (75%; n = 24), with an average direct medical cost of IDR 244.589. In contrast, the M-V combination was used in 25% of patients (n = 8) and was associated with a higher average cost of IDR 370.659. In this study, direct medical costs included drug costs, physician consultation fees, hospital facility utilization, and laboratory examinations. Direct medical costs refer to expenses incurred directly for healthcare services [30].

Table 3. Clinical effectiveness of m-g and m-v combination therapy.

Outcome measure	M-G (n=24)	M-V (n=8)	p
Baseline RPG (mg/dL), mean	223.79	251.38	
Follow-up RPG (mg/dL), mean	156.92	164.63	
Absolute RPG reduction (mg/dL), mean	66.88	86.75	
Percentage RPG reduction (%), mean	28.15	33.28	
Effective patients, n (%)	12 (50)	5 (62.5)	0.691
Ineffective patients, n (%)	12 (50)	3 (37.5)	

Note : RPG reduction (mg/dL) = Baseline RPG − Follow-up RPG. Percentage RPG reduction (%) = [(Baseline RPG − Follow-up RPG) / Baseline RPG] × 100. Patients were classified as effective if their individual RPG reduction was equal to or greater than the mean RPG reduction observed within the respective treatment group after one month of therapy.

Random plasma glucose (RPG) was used as the primary effectiveness outcome because this retrospective study was based on routinely collected medical records, in which HbA1c data were unavailable or inconsistently recorded for a substantial proportion of eligible patients. In contrast, RPG measurements were routinely documented during outpatient follow-up visits, allowing a more complete and comparable assessment of glycemic response across the study population. . Based on Table 3, M-V combination showed a numerically higher effectiveness than the M-G combination (62.5% vs. 50.0%), corresponding to an absolute difference of 12.5 %. Furthermore, Fisher's exact test showed that the difference in effectiveness between the two treatment groups was not statistically significant (p= 0.691). Although the M-V combination demonstrated a higher observed effectiveness, it was also associated with a higher average direct medical cost (IDR 370,659 vs. IDR 244,589). Subsequently, the ACER and the ICER were calculated. ACER represents the average cost per unit of therapeutic effectiveness gained [31]. In contrast, the ICER is an economic evaluation measure that calculates the additional cost required to obtain an additional unit of effectiveness from one intervention compared with an alternative therapy. ICER serves as a basis for determining whether an intervention provides *value for money* [32], [33].

Table 4. Average cost-effectiveness ratio.

Drug name	ACER
M-G	IDR 4.891,78
M-V	IDR 5.930,54

Table 5. Incremental cost-effectiveness ratio.

Comparison	Incremental cost (IDR)	Incremental effectiveness (%)	ICER (IDR / additional % of effectiveness)
M-G VS M-V	126,070	12.5	10.085,60

Based on Table 4, the ACER analysis showed that the M–G combination had a lower average cost-effectiveness ratio (IDR 4.891,78) compared with M–V (IDR 5.930,54). The M-G regimen yielded a lower ACER than the M-V regimen, indicating a lower average direct medical cost per percentage point of patients classified as effective. However, ACER provides only a descriptive measure of the average cost-effectiveness of each treatment regimen individually and should not be used as the primary basis for comparing mutually exclusive treatment alternatives. Accordingly, the comparative economic evaluation was primarily based on the Incremental Cost-Effectiveness Ratio (ICER), which quantifies the additional direct medical cost required to achieve one additional percentage point of treatment effectiveness when comparing the M-V regimen with the M-G regimen as the comparator. Meanwhile, the ICER value of IDR 10.085,60 indicates that each additional 1% increase in effectiveness achieved with M–V required an additional cost of IDR 10.085,60 compared with M–G.

Clinically, dipeptidyl peptidase-4 (DPP-4) inhibitors such as vildagliptin are known to have a more favorable safety profile with respect to hypoglycemia risk and are generally weight-neutral compared with sulfonylureas. Therefore, they are often considered for use in elderly patients or in those with cardiovascular comorbidities [34]. Recent meta-analyses have demonstrated that DPP-4 inhibitors provide glycemic-lowering efficacy comparable to that of sulfonylureas, but with a lower risk of hypoglycemia [10]. This finding is consistent with public healthcare system–based cost-effectiveness evaluations, which suggest that DPP-4 inhibitor–based therapy becomes cost-effective when reductions in severe hypoglycemia risk and improvements in long-term quality of life are considered, rather than when assessed solely on short-term direct medical costs. [35].

This study has several limitations. First, the retrospective design relied on routinely collected medical records, resulting in the use of random blood glucose rather than HbA1c as the effectiveness outcome. Second, the relatively small and unequal sample size may have reduced statistical power and increased uncertainty in the ICER estimates. Third, only direct medical costs from the hospital provider perspective were included. Finally, clinical outcomes such as hypoglycemia, body weight, cardiovascular events, and quality of life were not evaluated and therefore were not incorporated into the economic evaluation.

▪ CONCLUSION

Based on the data from this study involving outpatients with T2DM at Dr. Soekardjo Regional Public Hospital, it can be concluded that the M-V combination was 12.5% more effective than M-G. The average direct medical cost for M–G was IDR 244.589, while for M–V it was IDR 370.659. The ACER values were IDR 4.891,78 for M–G and IDR 5.930,54 for M–V, whereas the ICER was IDR 10.085,60. Overall, the M–V combination was more cost-effective, with each additional 1% increase in effectiveness requiring an additional cost of IDR 10.085,60.

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