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COST-UTILITY ANALYSIS OF METFORMIN AND GLIQUIDONE IN PATIENTS WITH TYPE 2 DIABETES MELLITUS AT A REGIONAL HOSPITAL IN INDONESIA

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ABSTRACT

Type 2 diabetes mellitus (T2DM) is a chronic disease requiring lifelong treatment and imposing a considerable economic burden on healthcare systems. This study aimed to evaluate the cost–utility of metformin and gliquidone therapy among patients with T2DM treated at a regional hospital in Indonesia. An analytical observational study with a cross-sectional design was conducted among 60 outpatients with T2DM between May and June 2025, including 40 patients receiving metformin and 20 receiving gliquidone. Direct medical costs were obtained from medical records, while health utility was assessed using the EQ-5D-5L questionnaire and converted into utility scores using the Indonesian EQ-5D-5L value set. Cost–utility analysis was performed using the Average Cost–Utility Ratio (ACUR) and Incremental Cost–Utility Ratio (ICUR), with health utility scores as the effectiveness outcome. Metformin therapy demonstrated lower direct medical costs than gliquidone (IDR 140,225 vs IDR 183,687). Mean utility scores were 0.776 and 0.749, respectively. Metformin produced the lowest ACUR (IDR 180,703 per utility score), whereas gliquidone showed an ACUR of IDR 245,243 per utility score. Incremental analysis indicated that gliquidone incurred higher treatment costs while providing lower health utility than metformin, indicating that gliquidone was economically dominated by metformin. Overall, metformin demonstrated the most favorable cost–utility profile and remains the preferred first-line therapy for patients with T2DM, while gliquidone may be considered in selected clinical conditions.
Keywords: Type 2 Diabetes Mellitus, Cost-utility Analysis, Metformin, Gliquidone, EQ-5D-5L

INTRODUCTION

T2DM is among the most common chronic metabolic disorders globally and has become a major public health concern because of its increasing prevalence and the risk of long-term complications. According to the International Diabetes Federation (IDF), approximately 537 million adults worldwide were living with diabetes in 2021, and this number is projected to increase to 643 million by 2030 and 783 million by 2045. More than 75% of people with diabetes reside in low- and middle-income countries (Magliano et al., 2021). In Indonesia, T2DM contributes substantially to morbidity, mortality, and healthcare expenditure,

particularly among adults and older populations (Kementerian Kesehatan Republik Indonesia, 2023).

The management of T2DM requires lifelong pharmacological therapy alongside lifestyle modification, which results in considerable economic burden for both patients and healthcare systems. Diabetes-related healthcare expenditure worldwide was estimated at approximately USD 966 billion in 2021, representing a 316% increase over the past 15 years (Magliano et al., 2021). In Indonesia, T2DM contributes substantially to healthcare utilization and expenditure due to the chronic nature of the disease and its associated complications. Oral antidiabetic drugs such as metformin and sulfonylurea derivatives are commonly prescribed as first- and second-line therapies due to their clinical effectiveness and wide availability (American Diabetes Association Professional Practice Committee, 2023). Metformin is generally recommended as first-line therapy because of its favorable efficacy, safety profile, and low cost, while gliquidone, a second-generation sulfonylurea, is often used as an alternative, particularly in patients with renal impairment (Perkumpulan Endokrinologi Indonesia, 2021).

Despite their widespread use, the selection of antidiabetic therapy should not be based solely on clinical outcomes but also on economic considerations and patient-reported outcomes, especially quality of life. Pharmacoeconomic evaluations play a critical role in supporting rational decision-making by comparing costs and health outcomes associated with alternative therapies (Rascati, 2014). Among the available pharmacoeconomic methods, cost–utility analysis (CUA) is particularly valuable because it incorporates patients' preferences for different health states through health utility values, enabling simultaneous evaluation of treatment costs and health-related quality of life (Drummond et al., 2015).

Health-related quality of life among patients with T2DM is frequently evaluated using validated instruments such as the EQ-5D-5L, which enables the measurement of utility values that can be applied in cost-utility analyses (Herdman et al., 2011). Numerous studies have shown that various antidiabetic therapies can produce similar clinical outcomes while differing in their cost-effectiveness and cost-utility profiles, emphasizing the need for economic evaluation when selecting appropriate treatment options (Anggriani et al., 2024; Sari et al., 2023).

In addition to clinical effectiveness, information regarding health-related quality

of life and economic consequences derived from real-world settings is essential to support evidence-based resource allocation. Cost–utility analysis, which incorporates health utility values derived from preference-based instruments such as the EQ-5D-5L, provides a comprehensive framework for evaluating the value of healthcare interventions by simultaneously considering both treatment costs and patient-reported outcomes. However, evidence regarding utility-based economic evaluation of oral antidiabetic therapies in Indonesian healthcare settings remains limited.

Although metformin and sulfonylurea derivatives are widely used in routine clinical practice, evidence regarding their utility-based economic outcomes in Indonesian settings remains limited, particularly in regional hospitals. Local real-world evidence is necessary because healthcare costs, prescribing patterns, and patient preferences may differ from those reported in other countries. Therefore, generating context-specific data may provide additional information to support efficient resource allocation and improve treatment decision-making. Accordingly, this study was conducted to assess and compare the cost-utility of metformin and gliquidone therapy among patients with T2DM at a regional hospital in Indonesia by utilizing the EQ-5D-5L instrument and the Average Cost-Utility Ratio (ACUR) method. The results of this study are expected to serve as evidence-based references for clinicians and policymakers in improving antidiabetic treatment strategies from both clinical and economic viewpoints.

METHODS

1. Study Design and Setting

This study utilized an observational study design with a cross-sectional approach to assess the cost-utility of oral antidiabetic therapy among patients with T2DM. The research was conducted at Banten Regional Hospital, Indonesia, which serves as a regional referral hospital. Data collection was carried out between May and June 2025, reflecting real-world outpatient clinical practice.

2. Perspective of Economic Evaluation

The economic evaluation was conducted from the healthcare provider perspective. Therefore, only direct medical costs related to outpatient treatment were included in the analysis, consisting of antidiabetic medications, concomitant medications, laboratory examinations, and medical service costs. Indirect costs and non-medical costs were not considered.

3. Study Population and Sample

The study population included outpatients diagnosed with T2DM who were

receiving oral antidiabetic treatment at Banten Regional Hospital during the study period. Data were collected from patients attending the outpatient clinic between 1 May and 30 June 2025. Patients who fulfilled the eligibility criteria were recruited using purposive sampling. The sample size was determined based on the number of eligible patients available during the study period. A total of 60 patients were recruited through purposive sampling to ensure that all participants met the predetermined inclusion criteria. Of these, 40 patients received metformin therapy, while 20 patients were treated with gliquidone, allowing for comparative cost-utility analysis between the two treatment groups.

4. Inclusion and Exclusion Criteria

Patients were considered eligible for inclusion if they were at least 18 years old, had a confirmed diagnosis of T2DM, and were treated with either metformin or gliquidone as monotherapy. In addition, all participants were required to possess complete medical records and provide written informed consent before enrollment in the study. Patients were excluded if they underwent combination antidiabetic therapy, had incomplete clinical or cost-related data, or experienced severe comorbidities that might significantly affect health-related quality of life outcomes.

5. Data Collection Procedures

Direct medical cost data were retrospectively obtained from patients' medical records, including expenses associated with antidiabetic medications and outpatient healthcare services. Meanwhile, health-related quality of life data were collected prospectively through direct patient interviews using the EQ-5D-5L instrument. The EQ-5D-5L assesses five dimensions of health status, namely mobility, self-care, usual activities, pain/discomfort, and anxiety/depression, and has been extensively applied in pharmacoeconomic research (Herdman et al., 2011).

6. Utility Measurement

Utility values were derived from patients' health states obtained using the EQ-5D-5L questionnaire and converted into utility scores using the Indonesian EQ-5D-5L value set developed by Purba et al. (2017). This approach enabled the utility estimates to reflect the health preferences of the Indonesian population. These scores reflect patients' preferences toward specific health conditions, with values ranging from 0, representing death-equivalent health status, to 1, indicating perfect health. Utility scores represented patients' preferences for their current health status and were used as the effectiveness outcome in the cost–utility analysis (Purba et al., 2017).

7. Cost-Utility Analysis

Cost-utility analysis was performed using both the Average Cost-Utility Ratio (ACUR) and Incremental Cost-Utility Ratio (ICUR). ACUR was calculated by dividing the mean direct medical cost by the corresponding health utility score value for each treatment group. In addition, ICUR was calculated to estimate the additional cost required to obtain an additional health utility score between alternative therapies using the following equation:

$$ICUR = \frac{CostA - CostB}{Utility\ A - Utility\ B}$$

The ICUR was interpreted according to the direction of incremental costs and utility outcomes. A therapy associated with higher costs and lower utility than its comparator was classified as economically dominated.

8. Statistical Analysis

Descriptive statistics were used to summarize patients' demographic characteristics, direct medical costs, and health utility scores. Continuous variables were summarized using means and ranges, while categorical variables were presented as frequencies and percentages. Cost and utility outcomes were descriptively compared between the metformin and gliquidone treatment groups. Cost–utility outcomes were subsequently evaluated using ACUR and ICUR. All data analyses were performed using SPSS.

Ethical Considerations

Ethical clearance for this study was granted by the Health Research Ethics Committee of Muhammadiyah University of Purwokerto with registration number KPEK/UMP/35/V/2025 prior to the commencement of data collection. All participants provided written informed consent after receiving a comprehensive explanation regarding the objectives and procedures of the study. In addition, the confidentiality and anonymity of patient information were rigorously protected throughout the research process.

RESULTS AND DISCUSSION

A total of 60 eligible outpatients with T2DM who met the predefined inclusion criteria during the study period were included in the analysis. Of these, 40 patients received metformin monotherapy and 20 patients received gliquidone monotherapy. The demographic characteristics of the study population are presented in Table 1. Female patients predominated in both treatment groups (58.3%), which is consistent with epidemiological data indicating higher healthcare utilization and longer life expectancy among women with T2DM (Hou

et al., 2024; Yu et al., 2025). Most participants were aged over 45 years, with the largest proportion in the 56–65 year age group (35.0%), reflecting the increasing prevalence of T2DM with advancing age due to progressive insulin resistance and β-cell dysfunction (Galicia-Garcia et al., 2020; Strati et al., 2024).

Table 1. Demographic characteristics of study participants

Characteristic	Metformin (n = 40)	Gliquidone (n = 20)	Total (n = 60)
Sex, n (%)			
Male	17 (42.5)	8 (40.0)	25 (41.7)
Female	23 (57.5)	12 (60.0)	35 (58.3)
Age group (years), n (%)			
36–45	6 (15.0)	2 (10.0)	8 (13.3)
46–55	14 (35.0)	6 (30.0)	20 (33.3)
56–65	13 (32.5)	8 (40.0)	21 (35.0)
>65	7 (17.5)	4 (20.0)	11 (18.3)

1. Direct Medical Costs and Their Implications

The analysis of direct medical costs demonstrated notable differences between the treatment groups (Table 2). Based on patient-level cost calculations, the mean total direct medical cost per patient was IDR 140,225 in the metformin group and IDR 183,687 in the gliquidone group. The observed difference in treatment costs was primarily associated with variations in antidiabetic medication costs and other healthcare resource utilization.

Table 2. Mean direct medical costs per patient by treatment group (IDR)

Cost Component	Metformin	Gliquidone
Antidiabetic medication	11,381	57,563
Other medications	20,190	18,541
Laboratory examinations	60,000	60,000
Nursing and medical services	100,000	100,000
Mean total direct medical cost per patient	**140,225**	**183,687**

These findings are in line with international pharmacoeconomic evidence identifying metformin as the least costly oral antidiabetic agent due to its widespread availability as a generic medication and inclusion in essential medicines lists across many healthcare systems (Babar et al., 2019; Saraswati et al., 2019). In contrast, second-generation sulfonylureas such as gliquidone are often reserved for specific clinical indications and may incur higher costs depending on procurement and

reimbursement mechanisms (Tomlinson et al., 2022).

From a health system perspective, cost differences of this magnitude are clinically relevant, particularly in publicly funded healthcare settings where budget constraints necessitate efficient allocation of resources. Previous studies have emphasized that even modest differences in per-patient cost can translate into substantial budgetary impact when extrapolated to large populations with chronic diseases such as T2DM (Alshowair et al., 2024; Butt et al., 2022).

The lower treatment cost observed in the metformin group is consistent with previous studies reporting that metformin remains one of the least expensive oral antidiabetic agents because of its widespread availability as a generic medicine and its inclusion in essential medicine lists. Similar findings have been reported by Saraswati et al. (2019) and Babar et al. (2019), who demonstrated that metformin is generally associated with lower acquisition costs than second-generation sulfonylureas. Consequently, metformin may represent an economically attractive option for healthcare systems facing budget constraints.

2. Health Utility Outcomes

Health-related quality of life, measured using the EQ-5D-5L instrument, revealed meaningful differences in utility outcomes among the evaluated therapies (Table 3). Patients receiving metformin monotherapy demonstrated the highest mean utility score (0.776), while gliquidone therapy yielded the lowest mean utility score (0.749). The observed utility scores ranged from 0.537 to 0.950 across the treatment groups and were comparable to utility values reported in previous studies of patients with T2DM using EQ-5D-based measures (Prabowo et al., 2023).

Table 3. Health utility values of patients receiving therapy

Parameter	Value	
	Metformin	**Gliquidone**
Number of patients (n)	40	20
Mean utility score (EQ-5D-5L)	0.776	0.749
Minimum utility score	0.537	0.537
Maximum utility score	0.950	0.950

The slightly lower mean utility observed in the gliquidone group may be attributable to treatment-related factors such as a higher risk of hypoglycemia and weight gain, both of which have been shown to negatively affect patient-reported quality of

life (Hougen et al., 2021; Seaquist et al., 2013). Conversely, metformin is generally associated with weight neutrality or modest weight loss and a lower risk of hypoglycemia, potentially contributing to more favorable utility outcomes (UK Prospective Diabetes Study Group, 1998).

The differences in utility scores among treatment groups may reflect variations in treatment tolerability and the risk of adverse events. Previous studies have demonstrated that hypoglycemia and weight gain associated with sulfonylurea therapy can negatively affect patients' health-related quality of life. Similar observations have been reported by Sari et al. (2023), who found differences in quality-of-life outcomes among patients receiving various oral antidiabetic therapies. Therefore, patient-reported outcomes should be considered alongside clinical efficacy when selecting antidiabetic treatment.

3. Cost–Utility Analysis and Interpretation

Average Cost–Utility Ratio (ACUR) analysis (Table 4) showed that metformin therapy had the lowest cost per utility score (IDR/utility score), indicating the most favorable cost–utility profile among the evaluated therapies. Gliquidone therapy produced a higher ACUR, reflecting greater treatment costs relative to the health utility achieved.

Table 4. Average Cost–Utility Ratio (ACUR) of antidiabetic therapies

Treatment Group	Mean Cost (IDR)	Mean Utility Score	ACUR (IDR/Utility Score)
Metformin	140,225	0.776	180,703
Gliquidone	183,687	0.749	245,243

These results are consistent with international economic evaluations that consistently identify metformin as a dominant or highly cost-effective first-line therapy for T2DM across diverse healthcare systems (Gkrinia et al., 2023). Although previous economic evaluations have sometimes positioned sulfonylurea-based therapies in trade-off quadrants, the present study placed gliquidone in the dominated quadrant because it was associated with higher costs and lower health utility than metformin (Davies et al., 2012).

The cost–utility diagram (Figure 1) further supports these findings by visually depicting the relative position of each therapy within the cost–utility plane. Metformin is positioned in the lower-cost and higher-utility region (Quadrant II, Dominant), whereas gliquidone is located in the higher-

cost and lower-utility region (Quadrant IV, Dominated). This indicates that metformin provides better health utility at a lower cost than gliquidone and therefore represents the economically preferred treatment option.

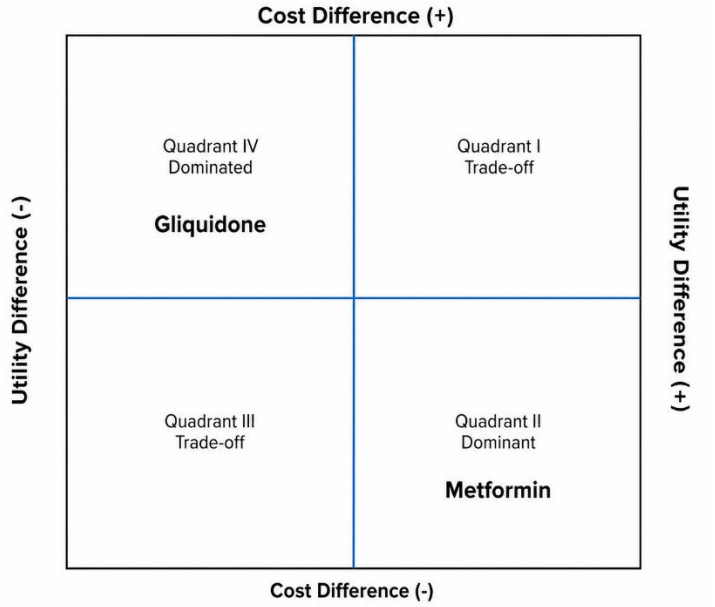

Figure 1. Cost–utility diagram between metformin and gliquidone

The present findings support previous economic evaluations indicating that metformin remains a highly efficient first-line therapy for T2DM. Davies et al. (2012) reported that therapies involving sulfonylureas may provide additional clinical benefits but are frequently associated with increased costs. Likewise, Gkrinia et al. (2023) concluded that treatment choices should consider both health outcomes and economic consequences to maximize healthcare resource allocation. Therefore, although alternative therapies may be appropriate in selected clinical situations, metformin remains the preferred option for most patients without contraindications.

Incremental cost–utility analysis was performed using metformin as the reference comparator. Gliquidone therapy incurred an additional mean cost of IDR 43,462 while producing a lower mean utility score (incremental utility = −0.027). Consequently, gliquidone was economically dominated by metformin because it was associated with higher costs and lower health utility.

Table 5. Incremental Cost–Utility Ratio (ICUR) of antidiabetic therapies

Comparison	Incremental Cost (IDR)	Incremental Utility Score	ICUR (IDR/Utility Score)
Gliquidone vs Metformin	43,462	-0.027	−1.609.704

In addition to ACUR, ICUR analysis was conducted to provide incremental evidence regarding the additional costs required to obtain additional health benefits. Compared with metformin, gliquidone therapy incurred higher treatment costs while producing lower health utility. Consequently, gliquidone was economically dominated by metformin, indicating that metformin represents the preferred treatment option from both clinical and economic perspectives.

These findings indicate that gliquidone was associated with higher treatment costs while producing lower health utility than metformin. Therefore, metformin represents the economically preferred therapeutic option. Incremental analysis is generally considered more informative for healthcare decision-making than average ratios because it evaluates the trade-off between additional costs and additional effectiveness.

4. Clinical and Policy Implications

From a clinical perspective, the findings reinforce current international guidelines that recommend metformin as the first-line pharmacological therapy for T2DM in patients without contraindications (Baker et al., 2021; Davies et al., 2012). Gliquidone and combination therapies may be appropriate alternatives in selected patients, such as those with contraindications to metformin or inadequate glycemic control, but their use should be carefully weighed against higher economic costs.

From a policy standpoint, these results provide locally relevant pharmacoeconomic evidence to support formulary decisions and reimbursement policies. Incorporating cost–utility evidence into decision-making processes may enhance efficiency in healthcare resource allocation, particularly in settings with limited budgets and a growing burden of chronic diseases.

These findings are also in agreement with recommendations from the American Diabetes Association and PERKENI, which identify metformin as the preferred initial pharmacological therapy because of its favorable balance between effectiveness, safety, and affordability. Gliquidone may serve as an alternative treatment, particularly in patients with contraindications to metformin or impaired renal function.

From a healthcare policy perspective, locally generated pharmacoeconomic evidence is important for supporting formulary management and efficient allocation of healthcare resources. Such evidence may assist policymakers in prioritizing interventions that provide the greatest health benefits relative to their costs, particularly in resource-constrained settings.

5. Study Limitations and Future Directions

Several limitations should be acknowledged. The cross-sectional design limits the ability to capture long-term changes in health utility. The relatively small sample size and single-center setting may restrict generalizability. In addition, no deterministic or probabilistic sensitivity analyses were conducted because the present study was based on observed cross-sectional data and did not employ decision-analytic modeling. Consequently, the robustness of the cost-utility estimates under varying assumptions could not be assessed. Future model-based economic evaluations are recommended to incorporate sensitivity analyses to improve the reliability of the findings. Additionally, the analysis was performed from the healthcare provider perspective and included only direct medical costs. Therefore, indirect costs and non-medical costs from the societal perspective were not captured, which may influence the overall cost–utility estimates.

Future research should employ longitudinal designs or decision-analytic modeling to evaluate long-term cost–utility outcomes using longitudinal or decision-analytic models and incorporate broader cost perspectives. Larger multicenter studies are also warranted to strengthen the evidence base for national-level policy formulation.

CONCLUSIONS

Metformin demonstrated the most favorable cost–utility profile among the evaluated antidiabetic therapies, with the lowest mean direct medical cost (IDR 140,225) and the highest mean health utility score (0.776). In contrast, gliquidone was associated with higher treatment costs (IDR 183,687) and a lower mean utility score (0.749), resulting in a less favorable Average Cost–Utility Ratio (ACUR). Incremental cost–utility analysis further indicated that gliquidone required additional healthcare expenditure while providing lower health utility than metformin, indicating that metformin remained the economically preferred treatment option. Therefore, metformin should continue to be considered the preferred first-line therapy for patients with type 2 diabetes mellitus, whereas gliquidone may be reserved for selected

clinical conditions in which metformin is contraindicated or not tolerated.

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