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Cost-effectiveness analysis of metformin and glimepiride therapy in patients with type 2 diabetes mellitus at cilongok i health center

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Abstract. Diabetes mellitus (DM) is a disease caused by disorders in the pancreatic organs that cause a decrease in the amount of insulin resulting in an increase in blood sugar. DM is the sixth leading cause of death in the world and the third in Indonesia. This metabolic disease is a disease that requires a lot of time and money in treatment. The treatment of diabetes mellitus needs to be taken into account because it costs a lot of money and causes a loss of productive time, so a Cost Effectiveness Analysis (CEA) is required. The study was conducted to determine the cost-effectiveness of the most effective single therapy of metformin and glimepiride in terms of benefits and costs in type 2 DM patients at the Cilongok I Health Center. The analysis was carried out by comparing the total cost incurred with the effectiveness of the therapeutic results obtained. The analysis of the cost effectiveness of therapy uses the Average Cost Effectiveness (ACER) calculation method in outpatient installations at the Cilongok I Health Center for the period of January 2024 – June 2024. Results: DMT2 patients who used metformin and glimepyride monotherapy, the statistical results showed that the most drug use was metformin and the analysis of metformin effectiveness had a lower ACER value of Rp. 798,136 with an effectiveness of 83.72% while glimepiride was Rp. 1,093,565 with an effectiveness of 72.72%. Conclusion: Based on the calculation of the ACER analysis method, the administration of metformin therapy alone is more cost-effective than glimepiride alone, the use of metformin as the main choice in the management of DMT2 can optimize health expenditure, improve the accessibility of care for patients and a sustainable and cost-effective treatment strategy.

1 Introduction

Diabetes mellitus that occurs in a person can be the sixth cause of death in the world and the third in Indonesia. Diabetes mellitus (DM) is chronic diseases in a person caused by disorders of the pancreatic organs that cause a decrease in the amount of insulin resulting in an increase in blood sugar and DM can be suffered for life (1). DM suffered by a person can also be caused by a decrease in pancreatic beta cells which is one of the causes of mitochondrial dysfunction, because mitochondria play an important role in the physiological stimulus-

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secretion relationship in beta cells. In these cells, mitochondria function as nutrient sensors and signal generators for insulin secretion. Specifically, the metabolism of mitochondrial pyruvate, which is derived from glucose through glycolysis, produces ATP, which in turn promotes the closure of K+ channels which is sensitive to ATP and subsequent cell depolarization, which induces the entry of Ca2+ through voltage-driven Ca2+ channels, an increase in the cytosol [Ca2+], and ultimately triggers insulin exocytosis (2).

Based on global prevalence data, it can be seen that diabetes mellitus is estimated to be around 422 million people and could increase to 642 million by 2040. Global health expenditure related to diabetes is estimated to reach 966 billion USD in 2021, and is projected to reach 1.054 billion USD by 2045. According to RISKESDAS data, the prevalence of DM disease in Central Java Province is 1.6% (3). The average handling cost per participant in Indonesia over the last five years (2018-2022) was IDR 912,538 and is expected to continue to increase to IDR 23.59 trillion in 2045 (4). The cost-effectiveness analysis of metformin and glimepiride therapy at the Cilongok I Health Center is very important considering the high burden of diabetes mellitus (DM) in Indonesia which is increasing every year, based on diabetes mellitus (DM) health services by sub-districts and health centers of Banyumas district/city in 2023, the highest number of DM sufferers was found at the Cilongok I Health Center as many as 1,650 patients.

Patients with diabetes mellitus can be treated through the administration of antihyperglycemic drugs. One of the most widely used drugs in Indonesia for diabetes mellitus is the administration of therapy with metformin followed by sulfonylurea drugs, especially glibenamide and glimepiride. Metformin and Glimepiride are two antidiabetic drugs that are often used in the treatment of diabetes mellitus. The mechanism of action of metformin decreases the concentration of blood sugar levels where the main mechanism of action is to lower glucose levels so that it causes a decrease in liver gluconeogenesis, in addition to metformin can be used monotherapy or in combination using one of the oral antihyperglycemic drugs, while glimepiride itself is a group of sulfonylureas that work to lower blood glucose levels by stimulating insulin secretion. Unlike other sulfonylurea groups, glimepiride is able to adjust the level of insulin secreted, especially in the *Post-dinner* so that the incidence of hypoglycemia is lower (5).

Diabetes mellitus, which is one of the diseases classified as metabolic, requires a lot of time and money in treatment. The length of treatment, the precision of therapy, patient compliance, and the amount of cost are all factors that affect the effectiveness of treatment (6).

Cost-effectiveness analysis is a necessary analysis in making decisions regarding the selection of effective drugs in terms of benefits and costs. The calculation of the cost effectiveness of therapy uses the Average Cost Effectiveness Ratio (ACER) and Incremental Cost Effectiveness Ratio (ICER) methods. To perform CEA, it is necessary to have data on the cost of treatment and the parameters of the effectiveness of the treatment or the outcome of the treatment. The medical cost in question is the direct cost incurred by the patient during treatment. The costs in question can include medical record fees, doctor consultation fees, medical equipment costs, laboratory fees, room fees and room service fees (for inpatients) (7).

Previous research that has been conducted at Robert Wolter Mongisidi Hospital, Manado City can be found that *effective* between metformin and glimepiride in the treatment of type 2 diabetes mellitus, namely metformin drug therapy with an ACER value of Rp. 49,156. Meanwhile, according to a study conducted in Yogyakarta on the cost-effectiveness between metformin and glimepiride, it is stated that glimepiride 2 mg is more cost-effective than the use of metformin 500 mg (8). The research at the Cilongok I Health Center aims to find out the comparison of *Cost-effective* Single antidiabetic treatment of metformin and glimepiride for PROLANIS (Chronic Disease Management Program) patients in the outpatient

installation of Cilongok I Health Center by analyzing the most common types of diabetes mellitus treatment *Cost-effective* for effective output reduction in GDP and the level of GD2JPP.

2 Materials and Methods

2.1 Study Design

This study is quantitative research with a retrospective observational design, using patient medical record data and applying inclusion and exclusion criteria for descriptive analysis. Inclusion of criterion 1 (PROLANIS patients with type 2 diabetes mellitus aged ≥ 18 years and routine PDB and GD2JPP laboratory examinations, using single therapy of metformin and glimepiride accompanied by comorbidities and without comorbidities, PROLANIS book data can be read clearly and completely including patient identity, profile of diabetes mellitus drug use (drug name, dose, duration), and the results of the GDP & GD2JPP audit). Exclusion Criteria (Patients with PROLANIS DM with incomplete medical record data, therapy used in combination with antidiabetics or single therapy with glibenclamide, acarbose, and gliquidone). Prior to the study, a pre-survey had been conducted at the Cilongok I Health Center with permit number 070.1/105/III/2024 from the Banyumas Health Office. This research has been approved and obtained permission from the Banyumas DPMPTSP to collect data with permit number 070.1/361/OL/VII/2024 and a code of ethics from Harapan Bangsa University with ethics number NO.B.LPPM-UHB/609/06/2024.

2.2 Sample and Data Collection

Sampling from the patient's medical record regarding name, age, type of drug, GDP level and GD2JPP level. Laboratory data results after the use of metformin and glimepiride therapy were recorded in patients who underwent routine laboratory examinations for 6 months from January to June 2024. Data on drug costs and administrative costs are obtained from the installation of pharmacies/pharmacies and the financial office of the Cilongok I Health Center for rates in accordance with regional regulation Number 1 of 2024 concerning "Regional Taxes and Levies".

Data collection was carried out by entering a research instrument sheet based on the PROLANIS book for outpatient type 2 diabetes mellitus patients at the Cilongok I Health Center, Banyumas Regency for the period January to June 2024.

2.3 ACER and ICER Value Calculation

ACER (average cost effectivenessness ratio) is a method used to analyze cost effectiveness and calculate the amount of costs that must be incurred. Cost savings with ACER are calculated based on the calculation of the total cost of direct treatment divided by the effectiveness of the therapy. Direct medical cost data can be used to calculate the Average CostEffectiveness Ratio (ACER) as shown in the formula below (9).

$$ACER = \frac{\text{Total Biaya Medis Langsung } (RP)}{Efektivitas\ (\%)}$$

ICER is a value that indicates the additional costs required to produce each change in a single unit of treatment outcomes. Cost savings are calculated by looking at the ratio of the cost difference between the two alternatives to the difference in effectiveness between the

two. The results of AEB can be concluded with the Incremental Cost-Effectiveness Ratio (ICER) as in the formula. If the ICER calculation results are negative or smaller, then alternative drugs are considered more effective and cheaper, so they can be used as recommendations for therapeutic options (9).

$$ICER = \frac{\text{Biaya A} - \text{Biaya B (Rp)}}{Efektivitas\ Terapi\ A\ (\%) - Efektivitas\ Terapi\ B\ (\%)}$$

3 Step

3.1 Dependent Variables

Metformin and glimepiride therapy in type 2 DM patients at the Cilongok I Health Center for the period January to June 2024.

3.2 Independent Variables

Cost-effectiveness analysis of metformin and glimepiride therapy in patients with type 2 DM.

4 Results And Discussion

4.1 Patient Characteristics

Table 1. Age frequency in patients with type 2 diabetes mellitus at Cilongok I Health Center (n: 65).

Patient Characteristics	Group	Frequency (f)	Presented (%)
Age	<45 years old	6	9,2
	>45 Years	59	90,8
Gender	Man	13	20
	Woman	52	80
Entire		**65**	**100**

In table 1 Data from the Cilongok I Health Center shows that 90.8% of type 2 diabetes mellitus patients aged >45 years are in line with a study at the South Purwokerto Health Center which noted that 97.5% of DM patients come from the >45 years age group which is a significant risk factor because hormonal changes and less active lifestyle can increase obesity and insulin resistance. Therefore, age is an important factor in the incidence of type 2 diabetes mellitus and needs to be considered in efforts to prevent and treat diabetes. (10).

The high incidence of type 2 diabetes mellitus in old age is due to age being the main risk factor for diabetes and prediabetes and is more likely to experience complications in the cardiovascular system, retina, and kidneys. As we age, the body's physiological functions will decline, including the pancreas, which can lead to impaired insulin action in target tissues and reduce insulin secretion by pancreatic beta cells in response to glucose (11).

The decrease in pancreatic beta cells is caused by mitochondrial dysfunction, as mitochondria play an important role in the physiological stimulus-secretion relationship in beta cells. In these cells, mitochondria function as nutrient sensors and signal generators for insulin secretion. In particular, mitochondrial pyruvate metabolism, which is derived from glucose through glycolysis, produces ATP, which in turn promotes the closure of ATP-

sensitive K+ channels and subsequent cell depolarization, which induces the entry of Ca2+ through voltage-driven Ca2+ channels, increasing [Ca2+cytosilic] and ultimately triggering insulin exocytosis (2).

In addition, age differences lead to changes in the socio-demographic picture and clinical characteristics. Hormonal and sedentary lifestyle changes in the elderly make the elderly more susceptible to obesity and increased insulin resistance, thereby increasing the risk of DM(10).

Based on the results of the research that has been carried out, it can be known in the gender category in table 1, namely the most type 2 diabetes mellitus patients in the Cilongok I Health Center are women as many as 52 patients (80%) compared to men as many as 13 patients (20%). This result is in line with previous research at the Sumbang Banyumas Regency Health Center which stated that women have a greater risk of developing type 2 diabetes mellitus than men (12). Women suffer from type 2 DM which is higher than men because in women there is a decrease in the hormone estrogen after menopause which causes the protection of the hormone estradiol to decrease in old age (13). Postmenopause can lead to the accumulation of lipids in the body through hormonal processes so there is a risk of an increase in a woman's body mass index and developing greater diabetes mellitus (14). In addition, most women are more at risk of developing diabetes mellitus because they are less involved in physical activity than men (12). Meanwhile, men have the hormone testosterone which is associated with a reduced incidence of type 2 diabetes mellitus. Meta-analysis research shows that higher testosterone levels may lower the risk of type 2 diabetes in men (15).

4.2 Patient diagnosis

Table 2. Patient Diagnosis

Diagnosis	Sum	Presented (%)
DM	52	80
DM+Hypertension	13	20
Entire	65	100

Based on table 2, it can be seen that there are 13 patients (20%) who have been diagnosed with DM type 2 disease with hypertension which can be seen from the increase in hypertension levels, where the normal value of blood pressure is ≤120 (mmHg). This is in line with previous research at Pertamedika Ummi Rosnati Hospital, Aceh City. The occurrence of hypertension in type 2 DM patients is caused by high blood sugar levels so that blood sugar sticks to the walls of blood vessels. This condition causes damage to the walls of blood vessels so that the walls of blood vessels become stiff, harden and result in blockages that cause changes in blood pressure called hypertension (16). Diabetes mellitus is also often associated with an event of insulin resistance that results in an increase in blood pressure, which can occur because insulin causes an increase in sodium retention which results in an increase in sympathetic nervous system activity (7).

The cause of insulin resistance in addition to the above factors can also be caused by improper activation of *Renin-Angiotensin-Aldosterone System* (RAAS). When RAAS is active, it will cause several mechanisms that result in an increase in BP becoming active. For example, angiotensin II, a product of RAAS activation, stimulates vasoconstriction and the production of aldosterone, the hormone responsible for salt and water retention in the kidneys that causes hypertension (17). In addition, the presence of secondary renal insufficiency due to diabetes can interfere with the ability to excrete water and solutes, cause excess fluid volume and improve the performance of the heart pump so that blood pressure continues to

increase (7).

4.3 Profile of therapeutic use

Table 3. Profile of Therapy Use

Antidiabetic drugs	Patient (n)	Percentage (%)
Metformin 500 mg	43	66,2
Glimepiride 2 mg	16	33,8
Glimepiride 4 mg	6	
Entire	**65**	**100**
Non-diabetic drugs		
Captopril	2	15,38
Amlodipine	5	38,46
Candesartan	6	46,15
Entire	**13**	**100**

Table 3 shows that metformin was used alone in 43 patients (66.2%), while glimepiride by 22 patients (33.8%) at Cilongok I Health Center (9).

The treatment of type 2 diabetes mellitus using the first line, metformin, results in a very dominant effect, namely the existence of a consistent preference in clinical practice (18). Treatment with metformin will reduce HbA1c levels by 1-2% so that it is more widely used for therapy. Metformin is indicated to be beneficial in overweight or obese patients, causing weight loss (2-3 kg). Metformin also has a positive effect on some components of insulin resistance syndrome and can lower plasma triglycerides and low-density lipoprotein cholesterol by about 8%-15%, and only increase high-density lipoprotein (HDL-C) cholesterol (2%) (19) ACE inhibitors are not only potent antihypertensive, but also show protective effects on certain organs, such as the kidneys, heart, and eyes as well as peripheral nerves in DM patients with hypertension. This effect is the result of inhibition of the hemodynamic effects and angiotensin I tissue (20).

4.4 Cost-Effectiveness

Pharmacoeconomics is a branch of health economics that focuses on weighing the costs and benefits of a particular intervention compared to Alternatives (21).

Table 4. Overview of Average Direct Treatment Costs for Type 2 DM Patients at Cilongok I Health Center

Types of fees	Average Cost (Mean)	
	Meformin	**Glimepiride**
Oral Antidiabetic Cost	236.177	411.545
Complication Costs	61.920	13.696
Consul and ADM Fees	10.000	10.000
Laboratory Fees	360.000	360.000
Total Cost	668.097	795.241

Table 4 can be seen that the direct treatment costs of DMT2 patients using glimepiride and metformin single oral therapy at the Cilongok I Health Center are as follows:

4.4.1 Oral anti-diabetic (ADO)

Oral antidiabetics (ADOs) are the costs used to pay for oral antidiabetics during treatment.

This fee is calculated based on the ADO unit price multiplied by the amount of daily usage provided during the treatment. Based on the table above, it is stated that the ADO price for metformin drug therapy is IDR 236,177, cheaper than the price of glimepiride drug therapy of IDR 781,545.

4.4.2 Complication Costs

Complication Fee is a fee used to pay for drugs other than ADO to overcome complications that occur due to diabetes suffered by patients. This cost is calculated based on the unit price of the drug multiplied by the number of uses per day given during treatment. Based on the table above, the total cost of metformin complications is Rp. 45,840 and glimepiride complications are Rp. 86,130. DM patients tend to have a history of comorbidities depending on the treatment of the disease, blood sugar level control and ADO provides unwanted side effects that cause complications that occur.

4.4.3 Consular and Administrative Fees

Consular and Administrative Fees are fees that must be paid for consultation services with doctors and registration administration, amounting to Rp. 10,000 at the Cilongok I Health Center according to the service levy rate at the Banyumas Health Center. Based on the table above, there is no significant difference in the consultation and administration costs of DMT2 prolanis patients between the consular and administrative costs of metformin and glimepiride, which is Rp 10,000 because it is subject to the same financing for each patient treated as an outpatient. Cost

4.4.4 Laboratory

Based on the table above, there is no significant difference in the laboratory cost of DMT2 patients between DMT2 patients who receive metformin and glimepiride monotherapy, namely Rp. 360,000 because the financing is the same for each patient who conducts laboratory examinations, the calculation method is that each outpatient DMT2 PROLANIS patient every month conducts laboratory examinations at a GDP rate of Rp.40,000 and GD2JPP Rp.20,000, and the data of this study are patients who routinely follow PROLANIS diabetes mellitus for 6 months, so the calculation method is by adding up the total GDP and the level of GD2JPP, then multiplying by 6 and obtaining a result of 360,000

4.4.5 Total Cost

The total cost is the total cost of the patient's therapy while undergoing DMT2 treatment, including Oral Antidiabetic Costs, Complication Costs, Consular and ADM Costs, and Laboratory Costs. The table above shows that the average total cost of therapy for the glimepiride group is higher, which is Rp 1,237,675 compared to metformin of Rp 652,017. The difference was due to the frequency, duration and cost of antidiabetics between the two therapy groups. The total average cost to calculate Cost-effectiveness. The total average cost of each therapy group was compared to the percentage of therapy effectiveness.

4.4.6 Direct Medical Costs and ACER value calculation

Table 5. Overview of the effectiveness and cost of Metformin and Glimepiride therapy in type 2 DM patients at Cilongok I Health Center

Drug therapy	Total direct medical expenses (Rp)	Effectiveness of therapy (%)	ACER Value
Metformin 500 mg	668.097	83,72	798.136
Glimepiride (2 mg and 4 mg).	795.241	72,72	1.093.565

Table 6. Comparison of Cost-Effective Relationships Between Therapies

Cost-effectiveness	Lower Costs	Same cost	Higher Costs
Lower Effectiveness	A ICER Calculation	B	C (Dominated) Glimepiride
Equal effectiveness	D	And	F
Higher Effectiveness	G (They dominate) Metformin	H	I ICER Calculation

Information:

A : Low effectiveness, low cost of drug therapy (ICER calculation).
B : Low effectiveness, the cost of drug therapy is the same
C : Low effectiveness, high (dominant) drug therapy costs.
D : Same effectiveness, low cost of drug therapy
And : Same effectiveness, same cost of drug therapy
F : Same effectiveness, high cost of drug therapy
G : High effectiveness, low cost of drug therapy (dominant).
H : High effectiveness, same cost of drug therapy
I : High effectiveness, high cost of drug therapy (ICER calculation).

Table 5 shows that the lowest total direct treatment cost is in the use of metformin drug therapy, the cost incurred is Rp. 668,097 with an ACER value of Rp. 798,136., while the administration of glimepiride therapy is the highest total direct treatment cost with a cost of Rp. 795,241 with an ACER value of Rp. 1,093,565. This is due to the difference in drug prices between metformin and glimepiride, dosage requirements, and frequency of use and duration of treatment.

This result is in line with research conducted at Robert Wolter Mongisidi Hospital, Manado City in the period January – December 2021. In the study, it can be found that the highest ACER value was obtained in the therapy of the use of glimepiride with a result of Rp 73,718 and the lowest was the therapy of the use of metformin, which was Rp 49,156. The smaller the ACER value, the more cost-effective the drug is, so it can be concluded that metformin is a cost-effective drug for antidiarrheal therapy in patients at Robert Wolter Mongisidi Hospital, Manado City (9).

Table 6 can be seen that the drug therapy group A (Metformin) is more effective and the cost cheaper so that it is included in the dominant category and does not require ICER

calculations. ICER calculations can be done if therapy Medications are more expensive but more effective or therapy costs less expensive but less effective. ICER can be used to explain the amount of additional costs for each health improvement unit (22).

The results on the cost-effectiveness diagram can be seen that the dominant column is the opposite of the dominant column, which means that when there is a comparison of therapies located in the dominant column while in the dominant column there is also a comparison of therapies, then the automatic use is the comparison that is in the dominant column. Therefore, the alternative therapy option for the use of single oral antidiabetic in PROLANIS DMT2 patients at the Cilongok I Health Center is Metformin.

5 Conclusion

Research at the Cilongok I Health Center showed that the Average Cost Effectiveness (ACER) of the use of metformin single therapy proved to be more cost-effective than glimepiride, with a cost of Rp 798,136 and an effectiveness of 83.72%, compared to glimepiride which had a cost of Rp 1,701,973 and an effectiveness of 72.72%. The use of metformin can be used as a recommendation for the treatment of type 2 diabetes mellitus because pharmacoeconomically, metformin therapeutic treatment is more cost-effective. The use of metformin as the primary choice in the management of DMT2 can optimize health expenditures, improve the accessibility of care for patients and sustainable and cost-effective treatment strategies. It is hoped that all health facilities in Indonesia can maintain the metformin treatment budget for type 2 diabetes mellitus effectively and efficiently.

Reference

1. Lestari, Zulkarnain, Sijid SA. Diabetes Melitus: Review Etiologi, Patofisiologi, Gejala, Penyebab, Cara Pemeriksaan, Cara Pengobatan dan Cara Pencegahan. UIN Alauddin Makassar. 2021;(November):237–41.
2. Diane A, Al-Shukri NA, Bin Abdul Mu-u-min R, Al-Siddiqi HH. β-cell mitochondria in diabetes mellitus: a missing puzzle piece in the generation of hPSC-derived pancreatic β-cells? J Transl Med. 2022;20(1):1–10.
3. Kemenkes RI. Laporan Riskesdas 2018 Nasional.pdf. Jakarta: Kementerian Kesehatan Republik Indonesia; 2018.
4. IDF. Biaya Penanganan Diabetes di Indonesia Diproyeksikan Meningkat 33 % pada 2045. 2021;(Per):2045.
5. Fahmi NF, Firdaus N, Putri N. Pengaruh Waktu Penundaan Terhadap Kadar Glukosa Darah Sewaktu Dengan Metode Poct Pada Mahasiswa. Jurnal Nursing Update. 2020;11(2):1–11.
6. Sari DF, Kurniasih KI. Cost Minimalyzation Analysist Penggunaan Antidiabetik Metformin Dan Glimepirid Pada Pasien Diabetes Melitus Di Puskesmas Cimanggu 1. Seminar Nasional Penelitian dan Pengabdian Kepada Masyarakat (SNPPKM). 2023;265–71.
7. Lorensia A, De Queljoe D, Swari Santi MD. Cost-Effectiveness Analysis Kloramfenikol Dan Seftriakson Untuk Pengobatan Demam Tifoid Pada Pasien Dewasa Di Rumah Sakit Sanglah Denpasar. MPI (Media Pharmaceutica Indonesiana). 2019;2(2):105–12.
8. Rajasa DFY. Cost Effectiveness Analysis Penggunaan Metformin Dan Glimepirid Pada Terapi Diabetes Melitus Tipe 2 Pada Pasien Rawat Jalan Di Puskesmas Bantul 2 (Doctoral dissertation, Universitas Muhammadiyah Yogyakarta). 2023.

9. Meliawati NW, Lolo WA, Rundengan GE. Cost-Effectiveness Analysis of the Use of Metformin and Glimepiride in Patients With Type 2 Diabetes Mellitus Inpatient At the Hospital . Robert Wolter Mongisidi Manado City. Pharmacy Medical Journal. 2023;6(1):68–76.
10. Rakhmawati A. Korelasi Kadar Glukosa Darah Dengan Kolesterol Total Pada Pasien Diabetes Melitus Tipe 2 Di Puskesmas Purwokerto Selatan. Jurnal Bina Cipta Husada Vol. 2024;XX(2):32–41.
11. zhou. Age-related impairment of pancreatic beta-cell function: Pathophysiological and cellular mechanisms. Front Endocrinol (Lausanne). 2014;5(SEP):1–8.
12. Burkon LK, Nafisahh Nafisah, Prasetyo Tri Kuncoro, Dwi Arini. Efektivitas Buku Saku Sebagai Media Edukasi Dalam Meningkatkan Pengetahuan Diet Dan Kepatuhan Diet Pasien Diabetes Mellitus Tipe 2 Di Kecamtan Sumbang Banyumas. Prosiding Seminar Nasional dan Call for Papers. 2023;13(1):204–12.
13. Lemieux CL, deGroh M, Gibbons L, Morrison H, Jiang Y. A Tool to Assess Risk of Type 2 Diabetes in Canadian Adults. Can J Diabetes. 2020;44(5):445–7.
14. Jannah et al. 2021. Analisis Efektivitas Biaya Penggunaan Antidiabetik Oral Pada Pasien Diabetes Mellitus Tipe 2 Rawat Jalan Peserta Bpjs Di Rsud Bumiayu 2020. Pharmacy Peradaban Journal. 2021;1(2):20–9.
15. Yao QM, Wang B, An XF, Zhang JA, Ding L. Testosterone level and risk of type 2 diabetes in men: A systematic review and meta-analysis. Endocr Connect. 2018;7(1):220–31.
16. Marzuk RH, Oetari RA, Hanifah IR. Analisis Efektivitas Biaya Terapi Metformin dan Glimepiride pada Pasien Diabetes Melitus Tipe 2 di RSUD dr. Darsono Pacitan Tahun 2019. Jurnal Ilmu Farmasi dan Farmasi Klinik. 2023;20(1):20.
17. Akalu Y, Belsti Y. Hypertension and its associated factors among type 2 diabetes mellitus patients at Debre Tabor general hospital, northwest Ethiopia. Diabetes, Metabolic Syndrome and Obesity. 2020;13:1621–31.
18. PERKENI. Pedoman Pengelolaan Dan Pencegahan Diabetes Melitus Tipe 2 Dewasa Di Indonesia. 2021;
19. Baker C, Retzik-Stahr C, Singh V, Plomondon R, Anderson V, Rasouli N. Should metformin remain the first-line therapy for treatment of type 2 diabetes? Ther Adv Endocrinol Metab. 2021;12:1–13.
20. Astari C. Pola Pengobatan Insulin dan Ace - Inhibitor pada Pasien Diabetes Melitus Tipe 2 dengan Hipertensi Terhadap Kontrol Glikemik dan Tekanan Darah. Sasambo Journal of Pharmacy. 2020;1(2):34–40.
21. Tonin FS, Aznar-Lou I, Pontinha VM, Pontarolo R, Fernandez-Llimos F. Principles of pharmacoeconomic analysis: The case of pharmacist-led interventions. Pharm Pract (Granada). 2021;19(1):1–10.
22. ADA. Standards of Care in Diabetes-2023 Abridged for Primary Care Providers American Diabetes Association. American Diabetes Association. 2023;41(1):1–28.