COST – EFFECTIVENESS ANALYSIS OF USING ANTIDIABETIC IN OUTPATIENT WITH TYPE 2 DIABETES MELLITUS

Kusumaningtyas Siwi Artini[1*], Tiara Ajeng L[2], Annisa Kusuma Wardhani[3]
Departement of Pharmacy / Duta Bangsa University of Surakarta[1], Departement of Pharmacy / Duta Bangsa University of Surakarta [2] , Departement of Pharmacy / Duta Bangsa University of Surakarta [3]
*Correspondence Email : kusumaningtyas@udb.ac.id

ABSTRACT

Type 2 diabetes Mellitus is a chronic disease that requires lifelong treatment. In the course of the disease, if blood sugar levels are not controlled, it can lead to complications of other diseases. The variety of antidiabetic drugs used in therapy can lead to differences in the cost effectiveness of therapy. The aims of this study is to analyze the cost-effectiveness of antidiabetic therapy in outpatients at Dr. Moewardi Hospital. Data collection in this study was carried out retrospectively using medical records of outpatients with type 2 diabetes mellitus and billing data from the hospital The data obtained were then presented descriptively and the ACER value was calculated for the 2 most widely used drug groups. The results of this study showed that 30 patients received a combination of Insulin Analog (Basal) + Insulin Analog (Prandial/Premixed) and and 11 patients received Insulin Analog (Basal/ Prandial/ Premixed). The percentage effectiveness of combination therapy Insulin Analog (Basal) + Insulin Analog (Prandial/ Premixed) was higher than Insulin Analog (Basal/ Prandial/ Premixed) (83.33 vs 72.72). The ACER value of Insulin Analog (Basal) + Insulin Analog (Prandial/ Premixed) (IDR 13.802,42) is lower than Insulin Analog (Basal/ Prandial/ Premixed) (IDR 18.356). Based on the cost effectiveness table, the combination of Insulin Analog (Basal) + Insulin Analog (Prandial / Premixed) is more effective so that the combination of Insulin Analog (Basal) + Insulin Analog (Prandial / Premixed) is more cost effective than Insulin Analog (Basal / Prandial / Premixed).

KEYWORDS antidiabetic, acer, cost-effectiveness, diabetes mellitus type 2, insulin

INTRODUCTION

Diabetes mellitus is a chronic disease that occurs due to metabolic disorders characterized by increased blood sugar levels (Kristina, Endarti, Andayani, & Widayanti, 2020). Diabetes mellitus usually occurs in patients with obesity or who have other risk factors such as unhealthy lifestyles, smoking, high blood pressure, dyslipidemia which can increase the risk of complications and reduce the quality of life of patients (Gonçalves et al., 2019). Indonesia has the 6th highest number of people with diabetes mellitus in the world (Webber, 2021). Based on data from the International; Diabetes Federation (IDF), there are 537 million patients diagnosed with diabetes mellitus and continues to increase every year, which is expected to be 643 million people in 2030 and 783 people in 2045 (Webber, 2021). In Indonesia alone, the reported prevalence of diabetes mellitus has increased to 10.9% with a prevalence of diabetes mellitus incidence at all ages in Central Java Province of 1.6% (Kementrian Kesehatan Republik Indonesia, 2018).

Type 2 diabetes mellitus is a disease that must be treated for life, therefore in the therapy of type 2 diabetes mellitus requires high awareness and discipline from patients to control blood sugar levels and other risk factors (Escobar et al., 2022). The first-line drug in the treatment of diabetes mellitus is metformin (Depkes, 2008). Glibenclamide is given if metformin does not have a good effect and insulin is recommended as a third line (Robert & Brown, 2018). However, drug selection in diabetes therapy is still tailored to the patient's medical condition. The high prevalence of type 2 diabetes mellitus and the variety of drugs used in therapy result in increased medical costs (T. Tamilselvan et al, 2017).

According to the International Diabetes Federation (IDF), the total cost of diabetes management reached USD 727 billion in 2017 and will continue to increase every year (Webber, 2021). In Indonesia, the estimated economic burden of diabetes mellitus is $1.27 M (Kementerian Kesehatan RI., 2020), and these costs can be higher due to limited access to health centers (Finkelstein, E. A., Chay, J., & Bajpai, 2014). In previous studies, the largest components of medical expenditure related to diabetes complications were cardiovascular disease (42.3% of total complication costs), nephropathy (23%) and eye complications (14%) (Javanbakht et al., 2011). In another study, it was stated that patients who showed uncontrolled clinical outcomes (64.5%) with average direct medical costs incurred by patients were IDR 489.005, and for controlled clinical outcomes showed better quality of life and lower costs (Ratnasari et al., 2020). To evaluate the effectiveness of type 2 diabetes mellitus treatment therapy, an economic evaluation based on cost and clinical parameters is needed. This study aims to analyze the cost-effectiveness of type 2 diabetes mellitus therapy using a hospital perspective.

RESEARCH METHOD

This research was conducted using a cohort study design and was carried out by collecting data retrospectively using medical record data of type 2 diabetes mellitus patients and billing data from the revenue management section in one of Dr. Moewardi hospitals in Central Java. Medical record data obtained will be processed to determine patient characteristics, types of drugs received, and effectiveness of therapy. The financial data obtained will be processed using the cost effectiveness analysis (CEA) method. The samples in this study were patients with type 2 diabetes mellitus who underwent outpatient care at Dr. Moewardi Surakarta Hospital who met the inclusion criteria:

(a) Type 2 diabetes mellitus patients who undergo outpatient care with age> 18 years
(b) Type 2 diabetes mellitus patients with or without comorbidities

(c) Type 2 diabetes mellitus patients routinely control 3 consecutive months and get the same treatment
(d) Complete patient medical record data

And the exclusion criteria are:
(a) Incomplete type 2 diabetes mellitus patient data
(b) Pregnant and breastfeeding type 2 diabetes mellitus patients

RESULT AND DISCUSSION

(A) Patient Characteristics

Based on data obtained from Dr. Moewardi Hospital Surakarta, there were 90 patients who met the inclusion criteria. Patient data was then categorized based on gender, age, duration of diabetes mellitus, occupation, and comorbidities. The distribution of patient characteristics can be seen in table 1.

Table 1. Characteristics of Type 2 Diabetes Mellitus Patients in the Outpatient Installation of Dr. Moewardi Hospital

Description	Amount	Percentage (%)
Gender		
Male	**48**	**53,33 %**
Female	42	46,67 %
Age		
26 – 35	2	2 %
36 – 45	9	10 %
46 – 55	21	23 %
56 – 65	**31**	**34 %**
≥ 65	27	30 %
Duration of Illness		
≥ 5 tahun	43	47,78 %
≤ 5 tahun	**47**	**52,22 %**
Job		
Tidak Bekerja	8	9%
Petani	5	6%
Pedagang	4	4%
Swasta	27	30%
ASN	**35**	**39%**
Pensiunan	11	12%
Diagonose		
Without Comorbidities	23	25,56%
With Comorbidities	67	74,44%

From table 1. Based on the patient's gender, it is known that males suffer the most from type 2 diabetes mellitus, namely 53.33%. This is in line with previous research where patients with male gender are more than women (Putra, Udayani, & Meriyani, 2017). Gender is an unmodifiable risk factor for type 2 diabetes mellitus (Kementerian Kesehatan RI., 2020). Men and women have an equal chance if the patient does not lead a healthy lifestyle, is obese and has other risk factors (Webber, 2021).

Based on the age of the patient, it is known that the prevalence of type 2 diabetes mellitus patients increases with increasing age range, namely in the age group 26 - 35 years as much as 2%, the age group 36 - 45 years as much as 10%, the group 46 - 55 years as much as 23%, the age group 56 - 65 years 31% and the age group ≥ 65 years

as much as 30%. This is because as we get older, some organ functions decrease (Ulhaq, Indrawijaya, & Suryadinata, 2023). With age, there will be a decrease in the sensitivity of pancreatic beta cells to incretin hormones and insulin resistance due to damage to pancreatic beta cells which causes the development of type 2 diabetes mellitus (Depkes, 2008). The data is in accordance with the data on the prevalence of type 2 diabetes mellitus by age group from the 2018 RISKESDAS data which states that the increasing age, the higher the prevalence of diabetes mellitus and the peak occurs at the age of 55 - 64 years and then decreases (Kementrian Kesehatan Republik Indonesia, 2018). The age that is prone to type 2 diabetes mellitus is above the age of 45 because at that age the risk of glucose intolerance increases which is related to the hormonal system of each individual (Soelistijo, 2021).

From the duration of type 2 diabetes mellitus, the most patients are patients with a duration of more than 5 years (52,22%). The prevalence of the duration of patients suffering from type 2 diabetes mellitus is in accordance with previously conducted research which states that the prevalence of type 2 diabetes mellitus duration is most prevalent in the group of more than 5 years (Ratnasari, Andayani, & Endarti, 2020). Diabetes mellitus is a degenerative disease that requires lifelong treatment (Soelistijo, 2021). The duration of diabetes mellitus diagnosis is a very influential factor in the occurrence of both macrovascular and microvascular complications (Perdana, Himayani, B, & Yusran, 2018). Diabetes mellitus is a silent disease and has an asymptomatic phase, which is the phase between the actual onset of diabetes hyperglycemia and the clinical diagnosis of diabetes mellitus (PERKENI, 2019).

Based on patient occupation data, it is known that the patient with the most diagnosed diabetes mellitus is ASN with a percentage of 39%. This data is in line with previous research where the percentage of ASNs as the most diabetes mellitus sufferers (Isnani, Muliyani, Zaini, & Arif Riyadi, 2021). The American Diabetes Association (ADA) states that a person who works has benefits in controlling blood glucose levels through physical activity and preventing complications (Association, 2022). Work factors affect the great risk of diabetes mellitus, work and light physical activity will cause a lack of energy burning in the body so that excess energy is stored in the body which will be stored in the form of fat which will cause obesity which is one of the risk factors for diabetes mellitus (Arania, Triwahyuni, Prasetya, & Cahyani, 2021).

The study found that the prevalence of diabetes mellitus with complications was prevalent (67%). This is in line with previous research which states that some people with type 2 diabetes mellitus experience complications (Fitria, Andela, Syaputri, & Nasif, 2023). As a silent killer, the incidence of diabetes mellitus is often not realized by patients and complications often occur, both chronic and acute complications (Dewi Prasetyani, 2017).

(B) Profile of Antidiabetic Drug Use

Drugs used in antidiabetic therapy consist of several classes either used singly or in combination. Antidiabetic drugs can be given orally or by injection. The drug profile used in this study can be seen in table 2:

Table 2. Profile of Antidiabetic Drug Use in the Outpatient Installation of Dr. Moewardi Surakarta Hospital

Antidiabetic Drug	Description	Amount	Precentage
Insulin Analog (Basal) + Insulin Analog (Prandial/ *Premixed*)	**Combination**	**30***	**33%**
Insulin Analog (Basal/ Prandial/ *Premixed*)	**Monotherapy**	**11***	**12%**
Biguanid	Monotherapy	10	11%

Biguanid + Sulfonilurea	Combination	10	11%
Biguanid + Penghambat DPP-4 + Insulin Analog (*Premixed*)	Combination	3	3%
Insulin Analog (Prandial) + Insulin Analog (*Premixed*)	Combination	3	3%
Sulfonilurea	Monotherapy	3	3%
Penghambat DPP-4 + Insulin Analog (Basal/*Premixed*)	Combination	3	3%
Sulfonilurea + Insulin Analog (*Premixed*)	Combination	2	2%
Sulfonilurea + Penghambat Alfa-Glukosidase	Combination	2	2%
Sulfonilurea + Biguanid + Insulin Analog (Basal)	Combination	2	2%
Penghambat DPP-4	Monotherapy	2	2%
Penghambat DPP-4 + Biguanid	Combination	1	1%
Penghambat Alfa-Glukosidase	Monotherapy	1	1%
Penghambat Alfa-Glukosidase + Insulin Analog (Prandial)	Combination	1	1%
Biguanid + Insulin Analog (*Premixed*)	Combination	1	1%
Biguanid + Sulfonilurea + Penghambat Alfa-Glukosidase	Combination	1	1%
Biguanid + Penghambat DPP-4 + Penghambat Alfa-Glukosidase	Combination	1	1%

Obat Antidiabetika	**Keterangan**	**Jumlah**	**Presentase**
Biguanid + Penghambat DPP-4 + Insulin Analog (Basal) + Insulin Analog (Prandial)	Combination	1	1%
Biguanid + Penghambat DPP-4 + Penghambat Alfa-Glukosidase + Insulin Analog (Basal)	Combination	1	1%
Penghambat DPP-4 + Insulin Analog (Basal) + Insulin Analog (Prandial)30	Combination	1	1%
	Total	90	100%

Based on the results of the study, it is known that there are 4 classes of drugs that are widely used in antidiabetic therapy, namely the combination of Insulin Analog (Basal) + Insulin Analog (Prandial / Premixed) 33%, Insulin Analog (Basal / Prandial / Premixed) 12%, Biguanid 11% and a combination of Sulfonylurea + Biguanid 11%. These results are in accordance with therapeutic guidelines from the guidelines for the management and prevention of adult type 2 diabetes mellitus in Indonesia (Soelistijo, 2021). The administration of antihyperglycemic drugs in accordance with the guidelines for type 2 diabetes mellitus therapy where as the first line the patient is given biguanide, then as the second line is the sulfonylurea group, if the administration of the biguanid and sulfonylurea groups does not provide therapeutic effects, the patient can be given insulin or a combination of antihyperglycemic drugs (Robert & Brown, 2018). These results are in accordance with previous research, namely the most widely used antidiabetic use is a combination of bolus and bolus insulin. The high provision of combination therapy is considered quite appropriate because it is in accordance with the PERKENI reference (Sembiring, Rahmawati, & Ramadhan, 2021).

(C) Cost - Effectiveness of Antidiabetic

(a) Effectiveness of Antidiabetic Therapy

The effectiveness of antidiabetic therapy used in this study is the average reduction in blood glucose of patients at the first visit and after 4 months of regular treatment. The glucose observed was fasting blood glucose. Based on the Guidelines for the Management of Type 2 Diabetes Mellitus in Indonesia, a person is said to have type 2 diabetes mellitus if the fasting blood glucose value is ≥ 126mg/dL or the blood sugar level 2 hours after eating ≥ 200mg/dL (Soelistijo, 2021). The decrease in blood sugar levels of patients who used the combination of Insulin Analog (Basal) + Insulin Analog (Prandial / Premixed) was 83.33% and patients who received Insulin Analog (Basal / Prandial / Premixed) was 72.72%.

(b) Avarage Cost Effectiveness

Avarage Cost Effectiveness Ratio (ACER) is a ratio that represents the unit cost of clinical outcomes calculated from the total cost of the program or treatment alternative divided by clinical outcomes (Andayani, 2013). Direct costs consist of costs that are directly tied to health care, including drug costs, polyclinic care costs and laboratory tests. The direct costs calculated in this study were the cost of antidiabetic drugs, administrative costs, doctor's fees, laboratory costs. The calculation of the Avarage Cost Effectiveness Ratio (ACER) of Antidiabetic Drug therapy in the outpatient installation of Dr. Moewardi Hospital can be seen in Table 3.

Table 3. Avarage Cost Effectiveness Ratio (ACER) of Antidiabetic Drug Therapy in the Outpatient Installation of Dr. Moewardi Hospital

Antidiabetic Drug	Average Total Direct Medical Cost (IDR)	Number Of Patients	Average Effectiveness (%)	ACER (IDR)
Insulin Analog (Basal) + Insulin Analog (Prandial/ *Premixed*)	IDR 1.150.155,97	30	83,33	IDR 13.802,42
Insulin Analog (Basal/ Prandial/ *Premixed*)	IDR 1.334.909	11	72,72	IDR 18.356

Based on the research data, it was found that patients who received a combination of Insulin Analog (Basal) + Insulin Analog (Prandial / Premixed) showed higher effectiveness than the group of patients who received insulin analog singly. From the calculation of ACER, the combined drug use of Insulin Analog (Basal) + Insulin Analog (Prandial / Premixed) is IDR 13,802.42 and Insulin Analog (Basala / Prandial / Premix) is IDR 18,356, meaning that the total average of the combination of Insulin Analog (Basal) + Insulin Analog (Prandial / Premixed) is lower than insulin analog (Basal / Prandial / Premixed). The ACER value indicates that 1% of effectiveness/outcome costs ACER. An intervention is concluded to be the most cost-effective if the ACER calculation value is smaller than other interventions. Based on this value, it can be concluded that the combination of Insulin Analog (Basal) + Insulin Analog (Prandial / Premixed) is more cost-effective than Insulin Analog.

The Cost-Effectiveness grid is used to describe the definition of 'cost-effectiveness'. To be able to declare a therapy or intervention more cost-effective, the cost and effectiveness of an intervention must be measured. The ACER values obtained were then interpreted into the Cost-Effectiveness grid to make it easier to draw conclusions. From the interpretation, it is known that the use of the combination of Insulin Analog (Basal) + Insulin Analog (Prandial / Premixed) is in cell G (dominant), namely with lower costs obtained higher effectiveness (J. Lyle Bootman, Raymond J. Townsend, 2005). ICER calculation can be done if an intervention costs more but its effectiveness is also high; or the cost of an intervention is lower but its effectiveness is also low (Andayani, 2013). This study did not calculate ICER because the combination therapy Insulin Analog (Basal) + Insulin Analog (Prandial / Premixed) was more dominant.

CONCLUSION

The conclusions of the research that has been carried out in outpatients suffering from type 2 diabetes mellitu include more male patients than female (53.33% vs 46.67%), the age range most suffering from type 2 diabetes mellitus (age 56 - 65 (34%), duration of illness more than 5 years (52.22%), with comorbidities 74.44%. The most widely used antidiabetic group was the combination of Insulin Analog (Basal) + Insulin Analog (Prandial / Premixed) (33%), Insulin Analog (Basal / Prandial / Premixed) (12%). The ACER value of Insulin Analog (Basal) + Insulin Analog (Prandial / Premixed) IDR 13,802.42 is lower than the ACER value of Insulin Analog (Basal / Prandial / Premixed) IDR 18,356 so that the use of a combination of Insulin Analog (Basal) + Insulin Analog (Prandial / Premixed) is more cost-effective than the single use of Insulin Analog (Basal / Prandial / Premixed).

REFERENCES

Andayani, Tri M. (2013). *Farmakoekonomi: Prinsip dan Metodelogi*. Yogyakarta: Bursa Ilmu Karangkajen.

Arania, Resti, Triwahyuni, Tusy, Prasetya, Toni, & Cahyani, Sekar Dwi. (2021). Hubungan Antara Pekerjaan Dan Aktivitas Fisik Dengan Kejadian Diabetes Mellitus Di Klinik Mardi Waluyo Kabupaten Lampung Tengah. *Jurnal Medika Malahayati*, *5*(3), 163–169. https://doi.org/10.33024/jmm.v5i3.4110

Association, American Diabetes. (2022). Standards of Medical Care in Diabetes-2022 Abridged for Primary Care Providers. *Clinical Diabetes : A Publication of the American Diabetes Association*, *40*(1), 10–38. https://doi.org/10.2337/cd22-as01

Depkes. (2008). *Pedoman Pengendalian Diabetes Melitus dan Penyakit Metabolik* (p. 82). p. 82. Retrieved from file:///D:/ebook/dsa664.pdf

Dewi Prasetyani, Sodikin. (2017). Analisis Faktor Yang Mempengaruhi Kejadian Diabetes Melitus (Dm) Tipe 2., *2*(2), 1–9.

Escobar, Carlos, Morales, Cristóbal, Capel, Margarita, Simón, Susana, Pérez-Alcántara, Ferran, & Pomares, Elisenda. (2022). Cost-effectiveness analysis of dapagliflozin for the treatment of type 2 diabetes mellitus in Spain: results of the DECLARE-TIMI 58 study. *BMC Health Services Research*, *22*(1), 1–9. https://doi.org/10.1186/s12913-022-07567-5

Finkelstein, E. A., Chay, J., & Bajpai, S. (2014). The economic burden of self-reported and undiagnosed cardiovascular diseases and diabetes on Indonesian households. *PLoS ONE*, *9*(6). Retrieved from https://doi.org/10.1371/journal.pone.0099572

Fitria, Najmiatul, Andela, Mila, Syaputri, Yolanda Zazna, & Nasif, Hansen. (2023). Analisis Efektivitas Biaya Penggunaan Metformin-GlimepirideTerhadap Penurunan Kadar Gula Darah Puasa Pada Pasien Diabetes Mellitus Tipe 2 di RS Universitas Andalas. *Jurnal Sains Farmasi & Klinis*, *9*(sup), 202. https://doi.org/10.25077/jsfk.9.sup.202-207.2022

Gonçalves, Ana Carolina Oliveira, Cazarim, Maurílio De Souza, Sanches, Cristina, Pereira, Leonardo Regis Leira, Camargos, Ana Márcia Tomé, Aquino, Jéssica Azevedo, & Oliveira Baldoni, Andre. (2019). Cost-effectiveness analysis of a pharmacotherapeutic empowerment strategy for patients with type 2 diabetes mellitus. *BMJ Open Diabetes Research and Care*, *7*(1). https://doi.org/10.1136/bmjdrc-2018-000647

Isnani, Nazhipah, Muliyani, Muliyani, Zaini, Muhammad, & Arif Riyadi, Muhammad. (2021). Analisis Efektivitas Biaya (Cost-Effectiveness) Penggunaan Antidiabetes Oral Kombinasi Pada Pasien Diabetes Melitus Tipe Ii Rawat Jalan Di Rsud Dr. H. Moch. Ansari Saleh Banjarmasin. *Jurnal Insan Farmasi Indonesia*, *4*(1), 103–110. https://doi.org/10.36387/jifi.v4i1.683

J. Lyle Bootman, Raymond J. Townsend, William F. McGhan. (2005). *Principles of Pharmacoeconomics*. USA: Harvey Whitney Books Company.

Javanbakht, Mehdi, Baradaran, Hamid R., Mashayekhi, Atefeh, Haghdoost, Ali Akbar, Khamseh, Mohammad E., Kharazmi, Erfan, & Sadeghi, Aboozar. (2011). Cost-of-illness analysis of type 2 diabetes mellitus in Iran. *PLoS ONE*, *6*(10), 1–7. https://doi.org/10.1371/journal.pone.0026864

Kementerian Kesehatan RI. (2020). Infodatin tetap produktif, cegah, dan atasi Diabetes Melitus 2020. *Pusat Data Dan Informasi Kementerian Kesehatan RI*, pp. 1–10.

Kementrian Kesehatan Republik Indonesia. (2018). Laporan_Nasional_RKD2018_FINAL.pdf. *Badan Penelitian Dan Pengembangan Kesehatan*, p. 674. Retrieved from http://labdata.litbang.kemkes.go.id/images/download/laporan/RKD/2018/Laporan_Nasional_RKD2018_FINAL.pdf

Kristina, Susi A. R. I., Endarti, D. W. I., Andayani, T. R. I. Murti, & Widayanti, Anna Wahyuni. (2020). Direct and Indirect Cost of Diabetes Mellitus in Indonesia: A Prevalence Based Study with Human Capital Approach. *International Journal of Pharmaceutical Research*, *13*(01). https://doi.org/10.31838/ijpr/2021.13.01.331

Perdana, Eva Narulita Kurnia, Himayani, Rani, B, Eka Cania, & Yusran, M. (2018). Hubungan Durasi Terdiagnosis Diabetes Melitus Tipe 2 dan Kadar HbA1C dengan Derajat Retinopati Diabetik pada Pasien yang Mengikuti Program Pengelolaan Penyakit Kronis di Puskesmas Kedaton Bandar Lampung. *Jurnal Majority*, *7*(2), 95–100. Retrieved from http://juke.kedokteran.unila.ac.id/index.php/majority/article/view/1857

PERKENI. (2019). Pedoman Pengelolaan Dislipidemi di Indonesia 2019. *PB. Perkeni*, 74.

Putra, I. Made Agus Sunadi, Udayani, Ni Nyoman Wahyu, & Meriyani, Herleeyana. (2017). Analisis Efektivitas Biaya Penggunaan Terapi Insulin Dan Insulin Kombinasi Pada Pasien Diabetes Mellitus Tipe Ii Rawat Jalan Di Rsup Sanglah. *Jurnal Ilmiah Medicamento*, *3*(2), 97–103. https://doi.org/10.36733/medicamento.v3i2.907

Ratnasari, Pande Made Desy, Andayani, Tri Murti, & Endarti, Dwi. (2020). Analisis Outcome Klinis Berdasarkan Kualitas Hidup dan Biaya Medik Langsung Pasien Diabetes Melitus Tipe 2. *Jurnal Sains Farmasi & Klinis*, *7*(1), 15. https://doi.org/10.25077/jsfk.7.1.15-22.2020

Robert, By, & Brown, E. Bob. (2018). *Guidelines on second-and third-line medicines and type of insulin for the control of blood glucose levels in non-pregnant adults with diabetes mellitus*. Geneva: World Health Organization.

Sembiring, Imanuel Saputra, Rahmawati, Dewi, & Ramadhan, Adam M. (2021). Analisis Efektivitas Biaya dan Minimal Biaya Pasien Diabetes Melitus Tipe 2 di RSUD Abdul Wahab Sjahranie Samarinda Tahun 2019. *Proceeding of Mulawarman Pharmaceuticals Conferences*, *14*(3), 173–178. https://doi.org/10.25026/mpc.v14i1.558

Soelistijo, Soebagijo Adi dkk. (2021). *Pedoman Pengelolaan dan Pencegahan Diabetes Melitus Tipe 2 Di Indonesia 2021*. Jakarta: PB. Perkeni.

T. Tamilselvan *, T. Kumutha, Amrita Lekshmi V., Anju C. James, Juliya S. Reji and Namitha Cheriyan. (2017). *Pharmacoeconomical Evalution Of Oral Hypoglicemic Agents For Type-2 Diabetes Mellitus In A Multuspeciality Hospital*. *8*(5), 2243–2248. https://doi.org/10.13040/IJPSR.0975-8232.8(5).2243-48

Ulhaq, Daffa Dhiya, Indrawijaya, Yen Yen Ari, & Suryadinata, Arief. (2023). Analisis Efektivitas Biaya Terapi Kombinasi Insulin dengan Obat Antidiabetes Oral pada Pasien Rawat Jalan Penderita Diabetes Melitus Tipe 2 di RSUD dr. Soehadi Prijonegoro Sragen. *Journal of Islamic Pharmacy*, *7*(2), 112–118. https://doi.org/10.18860/jip.v7i2.16376

Webber, Sara. (2021). International Diabetes Federation. In *Diabetes Research and Clinical Practice* (Vol. 102). https://doi.org/10.1016/j.diabres.2013.10.013