

Streamlining Oral Antidiabetic Prescribing Through Clinical Pathway Implementation

Susilo Ari Wardani^{1,2}

1. Master of Nursing, Universitas Muhammadiyah Yogyakarta, Indonesia
2. Dinas Kesehatan Provinsi Jawa Timur, Surabaya, 60231, Indonesia.

ARTICLE INFO

Submitted : 10-07-2024

Revised : 24-04-2025

Accepted : 29-04-2025

Published : 30-06-2025

Corresponding Author:
Susilo Ari Wardani

Corresponding Author Email:
susilo.ari.psc23@mail.umy.ac.id

ABSTRACT

Background: Diabetes mellitus (DM) is a disease that falls into the high-volume, high-risk, and high-cost categories. A concordance of oral antidiabetic drug prescribing with the clinical pathway (Pedoman Praktik Klinis, PPK) will ensure drug availability for patients in the universal coverage era.

Objectives: This study aimed to analyze the quantity and quality of antidiabetic drug use before and after PPK implementation, including concordance with the national formulary and PPK.

Methods: This cross-sectional study analyzes oral antidiabetic drug use for inpatient DM (ICD-10 E11) at Sumberlagah Regional Hospital, Mojokerto, East Java Province, Indonesia. Data were collected retrospectively from medical records and the pharmacy database. Drug utilization was presented in Defined Daily Dose per 100 bed-days descriptively.

Results: The quantity of inpatient DM drug use was 189.17 DDD/100 bed-days and 249.42 DDD/100 bed-days, before and after PPK implementation. The types of DM drugs that were included in the 90% DU category, before and after PPK implementation, were Insulin Aspart, Insulin Glargine, Glimepiride tablets, and Insulin Glulisine. The quality of DM drug use was 100% following the National Formulary 2022 and the PPK.

Conclusion: The oral anti-diabetic drugs in the 90% drug cumulative have great attention in the procurement to raise the financial efficiency. The DDD/100 bed-days of anti-diabetic and the number of items of anti-diabetic drugs are increasing, therefore necessitates proactive strategies to manage potential cost escalation for payers, i.e., The Government of Republic Indonesia.

Keywords: drug cumulative percentage; drug use study; quality of drug use

INTRODUCTION

Diabetes mellitus (DM), a metabolic illness, is characterized by persistent hyperglycemia due to disruptions in insulin production, activity, or both.¹ Systemic metabolic homeostasis disruption causes type 2 diabetes mellitus.² In 2017, estimates put the global prevalence of diabetes in adults aged 20 to 79 at 425 million, with forecasts indicating a 48% increase to roughly 629 million by 2045. The WHO predicts that the number of people with type 2 diabetes in Indonesia will rise from 8.4 million in 2000 to 21.3 million by 2030. Identification of patients at high risk of developing type 2 diabetes is critical owing to the requirement for early treatment, which can delay or even prevent disease progression.³⁻⁵

Although there is no cure for diabetes, therapy is required to keep blood glucose levels near normal. The overall objective of diabetes therapy is to enhance the quality of life for people with the disease. The short-term aims are to ease DM symptoms, improve quality of life, and lower the risk of acute complications, while the long-term goal is to avoid and slow the progression of problems. Healthy dietary habits and regular physical activity can help with DM therapy.⁶

Diabetes can cause both macrovascular and microvascular problems. These complications are the leading causes of morbidity and death, as well as a large burden on diabetes care.⁷ The American Diabetes Association (ADA) stated in May 2013 that the economic burden of DM treatment in the United States in 2012 was \$245 million, including \$176 million in direct medical expenses and \$69 million in indirect costs. In a study conducted at PKU Muhammadiyah Hospital Yogyakarta from January to June 2014, the highest direct medical costs incurred for type 2 DM patients with complications averaged IDR 556,378 ± 561,171, and the highest costs for inpatient care with complications averaged IDR 9,780,350 ± IDR 3,739,534 per inpatient period.⁸ The high incidence rate, risk of complications, and economic burden demand careful and reasonable treatment based on a clinical pathway (Clinical Practice Guidelines, *Pedoman Praktik Klinis* [PPK]).⁹⁻¹¹

A medical committee supervises and authorizes a group of medical personnel to develop PPK. Healthcare professionals incorporate PPK into their daily practices to enhance patient well-being and survival, enhance the quality of patient care, and remove unnecessary treatments.^{12,13} Adherence to PPK might potentially benefit patients, healthcare professionals, and the healthcare system by increasing treatment quality, lowering costs, minimizing inappropriate practice variations, and reducing avoidable side effects and mistakes.¹⁴ To eliminate variance in practice, a yearly review of medical staff performance is essential. According to Nugraha (2018), when doctors use PPK, there are fewer practice variances than when doctors do not use it.¹⁵ This demonstrates that following PPK guidelines may reduce practice variability while still ensuring quality control. One of the Drug Use Evaluation (DUE) entails determining the compatibility of drug items used with those contained in the PPK.¹⁰

DUE is an organized and continuous qualitative and quantitative procedure designed to assess the achievement of rational drug use. Compliance with the National Formulary (*Formularium Nasional*, *Fornas*) enables the early detection of irrational drug use. DUE also enables the early detection of five drug-related disorders.¹⁶⁻¹⁹ At one Yogyakarta academic hospital, drug usage compliance with the National Formulary was 64.57% in 2016 and 86.25% in 2019, with an average of 74.41%. These statistics indicate that drug use adherence to Fornas falls short of the hospital's basic service criteria, which require 100% compliance.¹⁶ Noncompliance with Fornas can have an impact on quality and cost control, as well as irrational medication usage and constraints on patient access to pharmaceuticals.²⁰⁻²²

Healthcare services use the National Formulary (Fornas), a collection of medications, as a reference for prescribing.^{17,21} Its goal is to improve the quality of healthcare services by increasing treatment efficacy and efficiency, resulting in sensible medication usage.²¹ Several variables might cause prescriptions to differ from Fornas, including a lack of communication between doctors and pharmacists, medical considerations (patient circumstances), and formulary changes.^{23,24} There is currently limited research comparing drug usage evaluations before and after PPK adoption. The aim of the study was to analyze the quantity and quality of DM drug use before and after PPK implementation in DDD/100 bed-days unit and 90% drug cumulative (DU90%); and to examine the concordance with national formulary and PPK in inpatient DM patients at Public Regional Hospital, Mojokerto.

METHODS

Study design

The study used an observational technique with retrospective data collection, patient prescription billing as the instrument, and both quantitative and qualitative methodologies.

Population and samples

The research population included all inpatient DM (Diabetes Mellitus) patients treated at RS X Mojokerto (total sampling) between January and March 2023, as well as July and September 2023. The sample includes DM inpatients at RS X Mojokerto who satisfied the inclusion criteria, i.e., patients over the age of 17, excluding those treated in the ICU or HCU, as well as those who died during the period before and after PPK implementation.

Study instruments

Drug consumption

The study used an observational technique with retrospective data collecting, patient prescription billing as the instrument, and both quantitative and qualitative methodologies.

The process of data collection involved extracting information from medical records, which included medical record numbers, patient demographics, and clinical data. We then used these records to search for patient prescription billing in the pharmacy installation. We collected the data in Excel and analyzed it to calculate

drug consumption. Using the DDD/100 bed-days unit, we computed the quantity of DM medication consumption as follows:

$$\frac{DDD}{100} \text{ bed-days} = \frac{\text{Total Drug (gram)} \times 100}{DDD WHO \text{ (gram)} \times LOS}$$

DDD WHO : Defined Daily Dose, a standard (average maintenance) dosage per day for adults (70kg) for its main indication.

LOS : Length of stays (days)

The DU 90% method conducts a quantitative examination of drug consumption by classifying it from highest to lowest, then determining the percentage and cumulative percentage of drug usage. The 90% segmentation is defined as the lowest cumulative percentage up to 90%.

Drug concordance

The concordance of DM medication use with the National Formulary (Fornas) were evaluated using the equations below.

$$\% \text{ The suitability of drug use with Fornas (National Formulary)} = \frac{\text{Number of medication items corresponding to Fornas}}{\text{Number of drug items used}} \times 100 \%$$

$$\% \text{ Compatibility of Drug Use with PPK} = \frac{\text{Number of medication items corresponding PPK}}{\text{Number of drug items used}} \times 100\%$$

Data Analysis

A descriptive analysis was used to identify samples' characteristics. T-tests were calculated to determine significant differences in means, and Pearson's Ch-q or Fisher's exact tests of correlations were computed to determine the strength and relations between variables. Student's t-test was used in comparison between two groups of quantitative variables. All statistical analyses were performed using the Statistical Package for Social Sciences, Version 22.0 for Window.

RESULTS AND DISCUSSION

Demographic and Clinical Characteristics

There were 99 samples before PPK implementation, from January to March 2023, and 133 samples after PPK implementation, from July to September 2023. Table 1 shows profiles of the samples' demographic and clinical characteristics. The samples in both periods were dominated by females, the pre-elderly age group, with service payment via BPJS and patient hospitalization length of < 5 days. Before the PPK implementation era, simple DM was the most prevalent diagnosis, but following the PPK implementation period, DM with many comorbidities took precedence.

The use of DM drugs had increased from 189.17 DDD/100 bed-days before PPK implementation to 249.42 DDD/100 bed-days after PPK implementation (Table 2) due to the number of patients comorbidities difference. The normality test showed that the data distribution was abnormal ($p < 0.005$). According to the Wilcoxon non-parametric test, there were statistically significant differences in drug consumption after PPK implementation ($p = 0.03$). The drugs that were the DU segmentation 90% before and after PPK implementation of PPK are insulin aspart, insulin glargine, glimepiride and insulin glulisine (Table 3). The concordance of DM medicine usage before and after PPK implementation with National Formulary 2022 is 100% and it is also 100% with PPK of Pathophysiology and Treatment of Diabetes Mellitus type II. The physician decision in prescribing antidiabetic in this study differ with prescribing pattern in India; combination of metformin and sulfonylurea was prescribed in 56% patients but insulin was underutilized.²⁵

Both before and after PPK implementation, women were the majority of DM patients at a public hospital in Mojokerto. Women²⁶⁻²⁸ and older adults²⁸ have a higher risk of developing diabetes mellitus compared to men. Women are more prone to obesity because of their greater fat content, which accounts for roughly 20–25% of their body weight, as opposed to males, who have a fat composition of 15-20%. According to RISKESDAS statistics from 2013, the prevalence of obesity in women is 32.9%, compared to 19.7% in males.

Table 1. Demographic and Clinical Characteristics of the Sample (N = 232)

Variable		Pre CP implementation (N=99)	Post CP implementation (N=133)
Sex	Male	27 (27.27)	41 (30.83)
	Female	72 (72.73)	92 (69.17)
Age	19-<45	10 (10.10)	14 (10.53)
	45-<60	48 (48.49)	65 (48.87)
	60-<70	31 (31.31)	46 (34.59)
	70≤	10 (10.10)	8 (6.01)
	<5	88 (88.89)	93 (69.93)
Length of stay (days)	5-<9	11 (11.11)	39 (29.32)
	9-19	0 (0.00)	1 (0.75)
Patient' diagnosis (ICD X)	E11.0	57 (57.58)	7 (5.26)
	E11.2	6 (6.06)	6 (4.51)
	E11.4	3 (3.03)	0 (0.00)
	E11.5	14 (14.14)	18 (13.53)
	E11.6	4 (4.04)	1 (0.75)
	E11.7	9 (9.09)	60 (45.11)
	E11.8	5 (5.05)	41 (30.84)
	E11.9	1 (1.01)	0 (0.00)

E11.0 Type 2 diabetes mellitus with hyperosmolarity, E11.2 Type 2 diabetes mellitus with kidney complications, E11.4 Type 2 diabetes mellitus with neurological complications, E11.5 Type 2 diabetes mellitus with circulatory complications, E11.6 Type 2 diabetes mellitus with other specified complications, E11.7 Type 2 diabetes mellitus with multiple complications, E11.8 Type 2 diabetes mellitus with unspecified complications, E11.9 Type 2 diabetes mellitus without complications

Table 2. Antidiabetic drugs density in DDD/100 bed-days

ATC			Post CP implementation	
Parenteral	A10AB05	insulin aspart	77.10	83.50
	A10AB06	insulin glulisine	18.69	14.65
	A10AD06	insulin degludec and insulin aspart	0.00	2.93
	A10AE04	insulin glargine	63.08	71.78
	A10AE05	insulin detemir	2.34	1.46
Oral	A10BA02	metformin	1.64	9.96
	A10BB08	gliquidone	2.96	4.69
	A10BB09	gliclazide	0.00	5.27
	A10BB12	glimepiride	23.36	54.00
	A10BF01	acarbose	0.00	0.59
	A10BG03	pioglitazone	0.00	0.59
Total			189.17	249.42

Diabetes patients are mostly over 45 years old. The loss of physiological function, particularly during the aging process, decreases organ function.²⁹ According to RISKESDAS 2013 statistics, the prevalence of diabetes increases with age and declines in the 65+ age group.

Compared to general payments, BPJS, specifically BPJS PBI (Recipient of Premium Assistance), is the primary source of payment for inpatient treatment. Diabetes mellitus is a chronic condition that demands large financial expenditures to control. In 2020, BPJS Kesehatan reported that money spent on DM claims climbed year after year, from IDR 6.5 trillion in 2018 to IDR 7.1 trillion in 2019, and will continue to rise to IDR 7.5 trillion in 2022.

Table 3. Percentage of drug cumulative (%DU)

ATC	Generic name	Pre CP implementation	ATC	Generic name	Post CP implementation
A10AB05	insulin aspart	40.76 (40.76)	A10AB05	insulin aspart	33.48 (33.48)
A10AE04	insulin glargine	33.35 (74.10)	A10AE04	insulin glargine	28.78 (62.26)
A10BB12	glimepiride	12.35 (86.45)	A10BB12	glimepiride	21.65 (83.91)
A10AB06	insulin glulisine	9.88 (97.90)	A10AB06	insulin glulisine	5.87 (89.78)
A10BB08	gliquidone	1.56 (97.90)	A10BA02	metformin	3.99 (93.77)
A10AE05	insulin detemir	1.24 (99.13)	A10BB09	gliclazide	2.11 (95.89)
A10BA02	metformin	0.87 (100.00)	A10BB08	gliquidone	1.88 (97.77)
			A10AD06	insulin degludec and insulin aspart	1.17 (98.94)
			A10AE05	insulin detemir	0.59 (99.53)
			A10BF01	acarbose	0.24 (99.76)

The Quantity of Diabetes Drug Use

Diabetes with complications now dominates DM, whereas simple diabetes predominated before PPK implementation. Insulin is the most widely utilized type 2 diabetes medicine among inpatients.³⁰⁻³² The Indonesian Endocrinology Association published a Guideline for the Management and Prevention of Type 2 Diabetes Mellitus. It advises treating people with type 2 diabetes who have extremely high-risk, high-risk, or chronic kidney disease (CKD) with SGLT-2 inhibitors, GLP-1, or insulin if these are not available.

Insulin aspart, a fast-acting insulin group, is the most often used diabetic medication, with DU levels of 90% before and after the trial. Individuals with inpatient diabetes mellitus require insulin treatment. The use of insulin allows healthcare practitioners to immediately modify the patient's blood sugar levels.

Quality of Diabetes Drug Use

Before and after PPK adoption, RS X Mojokerto ensured that medication use met the National Formulary and PPK for Diabetes Mellitus (ICD-10 E11). The National Formulary (Fornas) is a predetermined list of pharmaceuticals used as a reference in the administration of the National Health Insurance (JKN). Using Fornas as a drug reference can help patients utilize their medications more effectively, improve service quality, and manage treatment costs. Furthermore, it will assist pharmacists in planning and providing medications, improving service allocation efficiency.

The quality of DM medication usage before and after PPK deployment was fully compatible with Fornas 2022. This compliance is most likely since the pharmaceuticals offered in the pharmacy installation are all Fornas-compliant, leaving no room for prescribing physicians to prescribe prescriptions other than Fornas. According to Pratiwi et al. (2017), in one hospital in Bandung, 91.7% of prescriptions were for Fornas, with the remaining for pharmaceuticals other than Fornas delivered by the hospital pharmacy with hospital consent.²² This study indicates that by providing drugs outside of Fornas, prescribing physicians may be able to prescribe medications outside of Fornas, which can have an impact on the quality of drug services in the hospital because medication not included in Fornas is not part of the treatment package, resulting in additional costs for patients.

In early 2023, public hospital in Mojokerto changed its PPK, adopting the referral hospital's PPK. In June 2023, RS X Mojokerto began integrating the new PPK. After examining the quality of compliance with the usage of DM medicines with PPK, the findings revealed 100% compliance. Healthcare professionals' agreement to implement PPK and issue prescriptions in line with the PPK implementation, or the hospital's availability of DM drugs included in the PPK DM-RS, could explain this compliance. Unfortunately, the current PPK for DM only shows the drugs used in DM therapy and does not consider DM patients' associated disorders or comorbidities. According to Kurniati's (2017) research at RSU Aminah Blitar's Inpatient Unit, drug usage compliance was just 19%, and patients took medications other than the PPK offered in the hospital pharmacy.³² According to this study, administering medications outside of the PPK can result in lower compliance with drug use within the PPK, which can have an impact on patient quality of care and clinical outcomes.³²

CONCLUSION

All oral anti-diabetic drugs prescribed are on the formulary list and concordance with PPK. The oral anti-diabetic drugs in the 90% drug cumulative have great attention in the procurement to raise the financial

efficiency. All anti-diabetic prescribed in the research site are listed on the National Formulary and Clinical Guideline. The density of anti-diabetic and the number of items of anti-diabetic drugs are increasing. Anticipation should be made to contain the accelerating trends of cost from the perspective of payers, i.e. The Government of Republic Indonesia.

ACKNOWLEDGEMENT

The authors would like to thank Hospital's management and staffs for their assistance in conducting this research.

STATEMENT OF ETHICS

The study protocol (No. 895/3277/102.15/2023) was approved by the Ethical Committee of Rumah Sakit Umum Daerah Sumberlagah. Additionally, the study was conducted after review and written approval by the Administrational and Scientific Society of a public hospital in Mojokerto, according to the ethical standards of the Helsinki Declaration of 1983.

REFERENCES

1. Petersmann A, Müller-Wieland D, Müller UA, Landgraf R, Nauck M, Freckmann G, et al. Clinical Practice Guidelines: Definition, Classification and Diagnosis of Diabetes Mellitus. *Exp Clin Endocrinol Diabetes*. 2019;127(1):S1–7.
2. Demir S, Nawroth PP, Herzig S, Ekim Üstünel B. Emerging Targets in Type 2 Diabetes and Diabetic Complications. *Adv Sci*. 2021;8(18):1–23.
3. Laakso M. Biomarkers for type 2 diabetes. *Mol Metab*. 2019;27:S139–46.
4. Harreiter J, Roden M. Diabetes mellitus—Definition, classification, diagnosis, screening and prevention (Update 2019). *Wien Klin Wochenschr*. 2019;131(Update):6–15.
5. Soelistijo SA, Lindarto D, Decroli E, Permana H, Sucipto KW, Kusnadi Y et. al. Pedoman pengelolaan dan pencegahan diabetes melitus tipe 2 di Indonesia 2021. 2021;46.
6. Artasensi A, Pedretti A, Vistoli G, Fumagalli L. Type 2 Diabetes Mellitus : A Review of Multi-Target Drugs. 2020;1–20.
7. Cole JB. Genetics of diabetes mellitus and diabetes complications. *Nat Rev Nephrol*.
8. Amalia; Andayani, TM, Yuniarti E. Hubungan Komplikasi Diabetes Melitus Terhadap Biaya Terapi. 2015;159–70.
9. Ramdini DA. Evaluasi rasionalitas Penggunaan Obat Diabetes mellitus Tipe II Pada pasien Rawat Jalan Di Puskesmas Pasir Sakti Tahun 2019. *J Farm Lampung JFL*. 2020;(1):69–77.
10. Kementerian Kesehatan Republik Indonesia. Kepmenkes RI Nomor. HK.01.07/MENKES/1128/2022 tentang Standar Akreditasi Rumah Sakit April 2022.
11. Sutoto, Sastroasmoro S, Budiwaluyo W. Pedoman Penyusunan Panduan Praktik Klinis Dan Clinical Pathways Dalam Asuhan Terintegrasi Sesuai dengan Standar Akreditasi Rumah Sakit 2012. 2015;1–234.
12. Bierbaum M, Rapport F, Arnolda G, Nic Giolla Easpaig B, Lamprell K, Hutchinson K, et al. Clinicians' attitudes and perceived barriers and facilitators to cancer treatment clinical practice guideline adherence: A systematic review of qualitative and quantitative literature. *Implement Sci*. 2020;15(1):1–24.
13. Ryan MA. Adherence to Clinical Practice Guidelines. 2017;2–4.
14. Wang W, Choi D, Yu CH. Effective web-based clinical practice guidelines resources: recommendations from a mixed methods usability study. *BMC Prim Care*. 2023;24(1):1–10.
15. Nugraha NE. Implementasi Panduan Praktik Klinis Dalam Menurunkan Variasi Pelayanan Pada Tindakan Sectio Caesarea Di PKU Muhammadiyah Gamping. 2018;1–26
16. Adhi, Sigid Nugroho; Puspita Ningsih K. Manajemen Data Standar Pelayanan Minimal Rumah Sakit The Hospital Minimum Service Standard Data Management Studi Rekam Medis dan Informasi Kesehatan Fakultas Kesehatan Universitas Jenderal Achmad Yani Yogyakarta satunya adalah Standar Pelayanan Minimal Tu. 2020;3(2):53–62.
17. Kementerian Kesehatan Republik Indonesia. Kepmenkes RI Nomor. HK.01.07/MENKES/200/2020 tentang Pedoman Penyusunan Formularium Rumah Sakit. 2020;1–16.
18. Kementerian Kesehatan Republik Indonesia. Peraturan Menteri Kesehatan Republik Indonesia Nomor 72 Tahun 2016 Tentang Standar Pelayanan Kefarmasian Di Rumah Sakit. 2016;147(March):1–63.

19. Kementerian Kesehatan Republik Indonesia. Petunjuk Teknis Evaluasi Penggunaan Obat di Fasilitas Kesehatan. 2015;1–47.
20. Menteri Kesehatan Republik Indones. Menkes RI Nomor: 129/Menkes/SK/II/2008 tentang Standart Pelayanan Minimal Rumah Sakit. 2008;1–55.
21. Menteri Kesehatan Republik Indones. Permenkes RI Nomor 54 Tahun 2018 tentang Penyusunan dan Penerapan Formularium Nasional dalam Penyelenggaraan Program Jaminan Kesehatan. 2018;1–55.
22. Pratiwi WR, Kautsar AP, Gozali D. Hubungan Kesesuaian Penulisan Resep dengan Formularium Nasional Terhadap Mutu Pelayanan pada Pasien Jaminan Kesehatan Nasional di Rumah Sakit Umum di Bandung Relationship between the prescription suitability with the National of care in General Hospital i. 2017;00:48–56.
23. Pratiwi A. Evaluasi Kesesuaian Peresepan Obat Pada Pasien Bpjs Rawat Jalan Poli Penyakit Dalam Terhadap Formularium Nasional Di Rsud Kabupaten Bengkulu Selatan. 2020;
24. Sa'diyah H, Nuraini A. Profil Kesesuaian Peresepan Obat Pasien BPJS Dengan Formularium Nasional di Puskesmas Bangkalan Periode Januari-Maret 2020. *Indones J Pharm Herb Med*. 2021;1(1):5–9.
25. Lahiry S, Kundu A, Mukherjee A, Choudhury S, Sinha R. Analyzing Antidiabetes Drug Prescriptions With World Health Organization Anatomical Therapeutic Chemical/Defined Daily Dose Index to Assess Drug Utilization Pattern in Elderly Population of Rural Eastern India. *Indian Journal of Clinical Medicine*. 2017;8. doi:10.1177/1177393617703343
26. Tim Riskesdas 2018. Laporan Nasional Riskesdas 2018. Lembaga Penerbit Badan Penelitian dan Pengembangan Kesehatan. 2019;
27. Kautzky-Willer A, Harreiter J, Pacini G. Sex and Gender Differences in Risk, Pathophysiology and Complications of Type 2 Diabetes Mellitus. *Endocr Rev*. 2016;37(3):278-316. doi:10.1210/er.2015-1137.
28. Ciarambino T, Crispino P, Leto G, Mastrolorenzo E, Para O, Giordano M. Influence of Gender in Diabetes Mellitus and Its Complication. *Int J Mol Sci*. 2022;23(16):8850. Published 2022 Aug 9. doi:10.3390/ijms23168850.
29. Bellary, S., Kyrou, I., Brown, J.E. et al. Type 2 diabetes mellitus in older adults: clinical considerations and management. *Nat Rev Endocrinol* 17, 534–548 (2021). <https://doi.org/10.1038/s41574-021-00512-2>.
30. Coetzee A. An introduction to insulin use in type 2 diabetes mellitus. *S Afr Fam Pract* (2004). 2023;65(1):e1-e5. Published 2023 Apr 20. doi:10.4102/safp.v65i1.5702.
31. Emad-Eldin M, Balata GF, Elshorbagy EA, Hamed MS, Attia MS. Insulin therapy in type 2 diabetes: Insights into clinical efficacy, patient-reported outcomes, and adherence challenges. *World J Diabetes*. 2024;15(5):828-852. doi:10.4239/wjd.v15.i5.828.
32. Kurniati N 2017. Kesesuaian Pemberian Antibiotik Demam Tifoid Anak Di Unit Rawat Inap Rumah Sakit Umum Aminah Blitar Tahun 2017. *Amin Public Hosp Blitar*. 2017;8(1):1–12.