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Assessment to barriers of medication adherence among patients with Type 2 Diabetes Mellitus

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ABSTRACT: Medication adherence among diabetes mellitus (DM) patients in Indonesia was predominantly low or non-adherent. Poor adherence raises the risk of developing diabetes-related complications. Specific barriers contribute to the lack of adherence DM patients. The study aimed to identify barriers to medication adherence among DM patients in a primary healthcare center in Indonesia. The cross-sectional study was conducted in 27 primary healthcare centers in Banjarmasin, Indonesia. Patients with DM type 2 were recruited using a purposive sampling technique between February and March 2023. The Diabetes Medication Adherence Barriers Questionnaire (DMAB-Q) was used to assess barriers to medication adherence. A total of 455 patients with type 2 DM participated in this study. The results of the study found that there were various barriers to medication adherence. In terms of medication-related factors, symptoms that do not immediately improve (65,1%), side effects (55,4%), and the complexity of the medication regimen (58,9%) were reported. Regarding patient-related factors, lack of understanding of treatment goals (65,1%), negative perception of medication (53,0%), take medicine only when ordered by the pharmacist (32,5%), forgetting to take medication (28,4%), feeling bored, and feeling obligated to take medication every day (43,3%) were identified. As for pharmacist-related factors, the inability of patients to consult pharmacists promptly when encountering issues with their diabetes medication was prevalent (76,9%). Based on this study, it can be concluded that patient-related factors are the most dominant barriers to medication adherence among patients with diabetes mellitus.

KEYWORDS: Type 2 diabetes mellitus; adherence barrier; non-adherence; compliance; primary care.

1. INTRODUCTION

Diabetes mellitus is a medical condition marked by elevated blood glucose levels, which are brought on by issues with the body's production of the hormone insulin. The pancreas secretes insulin, which is involved in controlling blood glucose levels. A person with diabetes mellitus has problems with the body's ability to produce or use insulin effectively [1, 2]. If diabetes mellitus is not adequately controlled, it can have significant adverse effects on a patient's health. Long-term complications include heart problems, eye disorders, nerve damage, kidney issues, slow-healing wounds, and others [3, 4].

Nowadays, diabetes mellitus has become one of the most dangerous and prevalent chronic illnesses, lowering life expectancy and resulting in costly, incapacitating consequences. Diabetes mellitus is one of the global health issues that has experienced a significant increase in prevalence in recent decades. Data shows that the number of diabetes mellitus patients continues to rise in developed and developing countries [5-7]. According to data from the International Diabetes Federation (IDF), 537 million individuals worldwide had diabetes in 2021 [8]. According to estimates, the number of cases of diabetes in Indonesia will rise from 9,19% in 2020 (18,69 million) to 16,09% in 2045 (40,7 million), ranking it among the top 10 nations with the highest prevalence of type 2 diabetes and the steepest climb in rates [9, 10].

A comprehensive strategy is needed to manage diabetes mellitus, including adherence to medication recommendations, which include taking antidiabetic medication as directed by a physician and getting regular checkups to control blood glucose levels, as well as healthy lifestyle modifications like a balanced diet, regular exercise, stress reduction, and stress management. Preventing long-term consequences associated with this condition also requires strong coordination with the medical team, strict monitoring of blood glucose levels, patient education regarding disease management, and adherence to the drug regimen.

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A holistic approach that integrates these elements is crucial for effectively managing diabetes mellitus and preventing complications [11-13].

Adherence to medication plays a crucial role in the management of diabetes mellitus. Following the medication plan established by healthcare provider is a crucial factor in controlling this condition [14, 15]. When patients consistently adhere to the medication, it can help maintain blood glucose levels within a normal range, prevent long-term complications, and improve quality of life. Good adherence also allows healthcare professionals to conduct proper evaluations and provide necessary advice to tailor the care to the patient specific needs [16, 17].

A systematic review reported medication adherence rates ranging from 38.5% to 93.1%. Only 6 out of 27 studies (22.2%) reported medication adherence ≥ 80% within their study populations [18]. A Meta-analysis also reported a medication non-adherence proportion in diabetic patients across 8 studies averaging 37.8%, with a range of 25-91% [19]. A recent Systematic review and Meta-analysis published in 2023 indicated that the average medication adherence proportion among patient with diabetes mellitus across 156 studies was 54% [20].

From these data, it can be inferred that despite the variation in medication adherence proportions reported by various studies and analyses among patients with diabetes mellitus, there remains a significant challenge in achieving high levels of medication adherence within this population. The proportion of non-adherence or low adherence continues to be a significant issue, both globally and in Indonesia, highlighting the importance of enhancing support and adopting more effective approaches in managing medication among DM patients to achieve optimal control of the condition [21-23].

Low medication adherence in diabetes mellitus remains a crucial issue in Indonesia. A Systematic review based on 30 research findings in Indonesia found that medication adherence among diabetic patients was predominantly low or non-adherent [23]. Adherence to diabetes mellitus medication plays a vital role in improving therapeutic outcomes. Medication adherence helps control blood glucose levels, prevents dangerous fluctuations, and reduces the risk of long-term complications [24]. Identifying non-adherence in diabetes mellitus medication is essential to understand the challenges patients face and ensure adequate care [25]. Some factors that might contribute to this non-adherence include a lack of understanding or knowledge about diabetes mellitus and its treatment, financial difficulties in obtaining medications, disruptive medication side effects, confusion regarding complex medication regimens, issues with healthcare accessibility, or a lack of social support [26-29].

The antidiabetic medication adherence barrier level must be identified to improve therapy outcomes [30, 31]. However, there is limited information from research findings on barriers to diabetes mellitus medication adherence in Indonesia. One of the primary healthcare center facilities accessible to diabetes patients is the public health center (Puskesmas). Puskesmas is a government-managed healthcare facility that provides health services to the general public, including diabetes patients. The study aimed to identify barriers to medication adherence among diabetic patients in primary healthcare center in Indonesia. This research is needed to understand the factors preventing diabetic patients from adhering to medication. The results of this study are expected to serve as an evidence for healthcare professionals in developing healthcare approaches to optimize medication adherence among diabetic patients.

2. RESULTS

2.1 Profiles of barriers to medication adherence

The study's findings indicate that responses indicating 'never' were dominant in the domains of medication-related and patient-related factors, each comprising less than 80% of the responses. The high prevalence of 'never' responses indicates that certain items in the questionnaire are dominant barriers to adherence with diabetes medication. This underscores the significance of both medication-related and patient-related factors in influencing medication adherence among diabetes patients. Patients' responses to the DMAB-Q are summarized in Table 1.

Table 1. Factors related to barriers in diabetes medication adherence.

Domains	Statement	n (%)			
		Never	Sometimes	Often	Always
Medication-related factors	I stop taking medicine if I don't feel the benefit	296 (65.1)	117 (25.7)	27 (5.9)	15 (3.3)
	I increased the amount of medicine taken when there was no decrease in blood glucose levels	383 (84.2)	56 (12.3)	14 (3.1)	2 (0.4)
	I reduce the amount of medicine or stop taking medicine if I experience cold sweats/weakness/blurred vision	252 (55.4)	142 (31.2)	53 (11.6)	8 (1.8)
	I don't take medicine when I'm busy working	270 (59.3)	132 (29.0)	48 (10.5)	5 (1.1)
	I don't take medicine when traveling	268 (58.9)	129 (28.4)	52 (11.4)	6 (1.3)
	I have difficulty taking medicine several times a day	346 (76.0)	79 (17.4)	23 (5.1)	7 (1.5)
	I am having difficulty with transportation cost to take medicine at the Puskesmas	397 (87.3)	46 (10.1)	10 (2.2)	2 (0.4)
	I have no transportation to getting medicine at the Puskesmas	398 (87.5)	45 (9.9)	11 (2.4)	1 (0.2)
Patient-related factors	I only take medicine when my blood glucose levels were high	328 (72.1)	75 (16.5)	28 (6.2)	24 (5.3)
	I stopped taking medicine when the symptoms of diabetes had disappeared	296 (65.1)	95 (20.9)	41 (9.0)	23 (5.1)
	I stopped taking medicine because I felt there was no improvement in my health	330 (72.5)	89 (19.6)	26 (5.7)	10 (2.2)
	I stopped taking medicine because I was afraid it could cause kidney disorders	241 (53.0)	154 (33.8)	53 (11.6)	7 (1.5)
	I deliberately did not take medicine	358 (78.7)	81 (17.8)	15 (3.3)	1 (0.2)
	I take medicine only when ordered by the pharmacist	148 (32.5)	35 (7.7)	97 (21.3)	175 (38.5)
	I forgot to take my medicine	129 (28.4)	241 (53.0)	82 (18.0)	3 (0.7)
	I am forced to take medicine every day	297 (65.3)	117 (25.7)	28 (6.2)	13 (2.9)
	I'm tired of having to take medicine every day	197 (43.3)	185 (40.7)	58 (12.7)	15 (3.3)
Pharmacist-related factors	I didn't take medicine because I didn't understand how to take medicine explained by the pharmacist	391 (85.9)	52 (11.4)	9 (2.0)	3 (0.7)
	I don't take medicine because the pharmacist just handed me the medicine without providing information about medicine.	399 (87.7)	46 (10.1)	6 (1.3)	4 (0.9)
	I don't take medicine because I can't consult a pharmacist at any time if I have problems with medication	350 (76.9)	93 (20.4)	11 (2.4)	1 (0.2)
	I don't take medicine because the pharmacist doesn't have enough time to explain the medication	405 (89.0)	45 (9.9	1 (0.2)	4 (0.9)
	I don't take medicine because I don't believe the information given by the pharmacist	429 (94.3)	24 (5.3)	2 (0.4)	0 (0.0)

2.2 Demographic characteristics and diabetes medication adherence barrier level

A total of (n=455) patients were included in this study. The most of the patients were female, age 46-60 years, and have secondary level education. Approximately almost half of the respondents were unemployed. Most of the male and female patients reported have low adherence barriers. The other demographic like age, level education, and occupation were dominated by low adherence barriers also. The demographic variables of the patients and their correlation with diabetes medication adherence barrier level are summarized in Table 2.

Table 2. The correlation between demographic characteristics and diabetes medication adherence barrier level (n =455)

Patients' demographics		n (%)	Low barrier adherence	High barrier adherence	p value
Gender	Male	144 (31.6)	124 (86.1)	20 (13.9)	0.667
	Female	311 (68.4)	263 (84.5)	48 (15.5)	
Age (years)	18-45	62 (13.6)	57 (91.9)	5 (8.1)	0.102
	46-60	393 (86.4)	330 (83.9)	63 (16.1)	
Education	Uneducated	9 (2.0)	9 (100.0)	0 (0.0)	0.732
	Elementary	108 (23.7)	91 (84.2)	17 (15.8)	
	Junior high school	105 (23.1)	88 (83.8)	17 (16.2)	
	Senior high school	163 (35.8)	138 (84.6)	25 (15.4)	
	Undergraduate/Postgraduate	70 (15.4)	61 (87.1)	9 (12.9)	
Occupation	Government employee	50 (11.0)	44 (88.0)	6 (12.0)	0.653
	Private employee	78 (17.1)	68 (87.1)	10 (12.9)	
	Entrepreuner	99 (21.8)	87 (87.8)	12 (12.2)	
	Unemployed	228 (50.2)	188 (65.2)	40 (34.8)	

The study's findings reveal that 387 (85,1%) fall into the category of low barrier adherence. In Table 2, no differences were observed in patients' demographic characteristics based on the barrier adherence level. The chi-squared test indicated no statistical significance across all demographic characteristics. None of the demographic factors among diabetes patients, such as gender, age, education, and occupation, were significantly correlated with the barrier level of adherence to the diabetes regimen.

The medication-related factors, such as antidiabetic regimens and disease duration, were predominantly associated with low adherence barriers. As shown in Table 3, more than half of the patients received metformin as a single drug regimen. The majority of disease duration was one to five years. The chi-squared test indicated statistical significance between the level of diabetes medication adherence barriers and disease duration ($P < 0,05$). The Correlation between diabetes medication-related and diabetes medication adherence barrier levels are summarized in Table 3.

Table 3. The Correlation between diabetes medication-related and diabetes medication adherence barrier levels.

Diabetes medication-related		n (%)	Low barrier adherence	High barrier adherence	p value
Antidiabetic regimens	Glimepiride	27 (5.9)	26 (96.2)	1 (3.8)	0.394
	Glibenclamide	4 (0.9)	4 (100.0)	0 (0.0)	
	Metformin	244 (53.6)	203 (83.1)	41 (16.9)	
	Glimepiride and Metformin	138 (30.3)	118 (85.5)	20 (14.5)	
	Glibenclamide and Metformin	42 (9.2)	36 (85.7)	6 (14.3)	
Disease duration (years)	1-5	380 (83.5)	332 (87.3)	48 (12.7)	0.005
	6-10	64 (14.0)	48 (75.0)	16 (25.0)	
	>10	11 (2.5)	7 (63.6)	4 (36.4)	

3. DISCUSSION

Medication adherence is one of the determinants of treatment success, particularly for chronic diseases such as diabetes mellitus. The high prevalence of uncontrolled diabetes in healthcare services suggests that patients are non-adherent to their medication [27]. Patients with diabetes mellitus undergoing treatment in primary healthcare center settings often experience mild symptoms. These mild symptoms can often lead patients to not adhere to medication instructions [32, 33].

Various studies indicate that poor adherence to diabetes mellitus medication leads to treatment failure. Furthermore, treatment failure exacerbates the patient's clinical condition and leads to complications. Adherence to diabetes mellitus medication correlates significantly with blood glucose control. The higher level of adherence to diabetes mellitus medication, the better the blood glucose control [34-37]. It is critical to understand the causes of non-adherence in order to modify medication-taking behavior. Therefore, it is essential to investigate the barriers to medication adherence among patients with uncontrolled diabetes [38-40]. In this study, it was found that diabetes patients were predominantly characterized by low barrier adherence, yet this remains a cause of suboptimal diabetes treatment outcomes.

Most of the diabetic patients participating in our study showed that medication-related factors and patient-related factors are the most burdensome factors for medication adherence. In terms of medication-related factors, it was found that therapeutic effects that are not felt directly after taking the drug cause patients to predominantly exhibit non-adherence to medication. This may be because patients tend to feel that their symptoms have improved or are not too bothersome, leading them to ignore or reduce their medication dosage [41, 42]. The emergence of medication side effects during treatment is also a dominant factor causing patients to be non-adherence with medication. Patients tend to discontinue diabetes medication when experiencing such side effects. Furthermore, the complexity of the medication regimen is also a dominant factor hindering medication adherence. The obligation to take medication daily and the necessity to carry medication while traveling impose burdens on diabetic patients to comply with medication [43, 44]. Another studies conducted on diabetes mellitus patients in various countries showed similar results. They indicate that barriers to medication adherence are predominantly influenced by the emergence of side effects, the delayed onset of medication effects, and the complexity of medication regimens [40, 45-48].

In relation to patient-related factors, it was found that almost all factors are still burdensome barriers for diabetic patients to adhere to medication. Lack of patient understanding of treatment goals, negative perceptions of medication, psychologically depressed patient conditions, and poor medication behaviors contribute to inhibiting diabetic patients from adhering to medication. The Poor medication behavior includes using drugs based on personal assessment of the condition without considering pharmacist instructions and forgetting to take medication [27]. Patients do not fully comprehend their clinical conditions, the importance of medication, or the consequences of non-adherence to medication [49]. Patients who feel desperate or powerless tend to give up on their medication [50, 51]. These findings had similar results to other studies, they revealed that patient-related factors such as skipping doses of diabetes medication, forgetfulness, belief that prescribed medication is not helpful, lack of understanding of medication goals, and depression are commonly reported barriers to adherence [27, 40, 45, 52].

The adherence barriers in diabetes medication, encompassing both medication-related and patient-related factors, should ideally be minimized through the active involvement of pharmacists in providing pharmaceutical care for diabetic patients. Pharmaceutical care can serve as an effort to ensure that diabetic medication undergone by patients is appropriate, effective, and safe, thereby fostering patient adherence to the medication regimen [53, 54]. Pharmacists must be capable of identifying barriers to medication adherence in diabetic patients, enabling them to determine suitable interventions to enhance medication adherence in diabetic patients. Furthermore, pharmacist competency in implementing pharmaceutical care must constantly be improved to improve the quality of pharmaceutical care [55, 56].

In pharmacist-related factors, only one significant factor hindering adherence among diabetic patients was identified. This factor involves the inability of patients to consult pharmacists promptly when encountering issues with their diabetes medication. This limitation arises when diabetic patients undergo treatment at home, as they can only consult pharmacists when they visit healthcare facilities. Similar studies also found identical barriers from pharmacist-related factors. The suboptimal implementation of pharmaceutical care, limited time of meetings between pharmacists and patients have been identified as dominant barriers to medication adherence among diabetic patients [40, 52, 57, 58]. This barrier can be minimized by implementing telepharmacy services, allowing patients to interact with pharmacists in real-time to address medication-related issues without needing face-to-face encounters [59, 60]. Telepharmacy has been widely implemented to support the provision of pharmaceutical care in various countries [61, 62].

Medication adherence barriers consistently emerge across various demographics and characteristics of diabetic patients [63]. Research findings also indicate that the level of barriers to diabetes medication adherence does not correlate with patient demographics and nearly all diabetes medication-related factors, except for disease duration. Disease duration correlates with the level of barriers to diabetes medication

adherence. The longer the duration of diabetes mellitus, the higher the adherence barrier level in patients [64].

The results of this study indicate that medication non-adherence remains prevalent among diabetes mellitus patients worldwide, with similar barriers to adherence. These barriers mutually influence each other, leading to simultaneous effects that contribute to patient non-adherence. A comprehensive strategy is needed to address all barriers to medication adherence simultaneously, aiming to optimize outcomes in diabetes mellitus medication [65].

This study has limitations as it employs self-reporting methods to reveal barriers to medication adherence in diabetic patients. The subjectivity in patient assessments may affect the accuracy of the gathered data. Additionally, the questionnaire used does not collect sufficiently in-depth information about the socio-demographic characteristics of the respondents. The subsequent research is expected to develop various educational and behavioral interventions aimed at overcoming adherence barriers in medication for diabetes patients.

4. CONCLUSION

The investigation into primary healthcare has highlighted considerable barriers to medication adherence. Patient-related factors are the most dominant barriers to medication adherence among patients with diabetes mellitus. The most common barriers to adherence found in medication-related factors were side effects and the complexity of the medication regimen, in patient-related factor were lack of understanding of treatment goals and forgetting to take medication, meanwhile in the pharmacist-related factors was the inability of patients to promptly consult pharmacists when encountering issues with their diabetes medication.

5. MATERIALS AND METHODS

5.1 Study Setting and Design

This is a cross-sectional study conducted in 27 primary healthcare centers (Puskesmas) in Banjarmasin, Indonesia. Patients with diabetes mellitus were recruited as the research sample, and data collection was carried out in February - March 2023.

5.2 Inclusion criteria

Type 2 DM patients who were ≥18 years old, could communicate in Indonesian, and had been taking an antidiabetic drug for at least three months were eligible to be recruited.

5.3 Data collection

The researcher approached All eligible participants at the primary healthcare centers while they were waiting for their prescription medication. If they agreed to participate in the study, the researcher obtained informed consent. Individual interviews using a standardized questionnaire were conducted in person. The survey consisted of two sections. Part A included demographic information and data related to diabetes mellitus medication, such as inquiries about sex, age, occupation, education level, the number of antidiabetic medications, and the duration of diabetes mellitus. Part B comprised twenty-two questions in The Diabetes Medication Adherence Barriers Questionnaire (DMAB-Q).

5.4 Measurement

The DMAB-Q was developed for this research and was used to assess medication adherence barriers in diabetes mellitus patients. The questionnaire was developed based on three theoretical domain framework questions about patient related factors, medication related factors, and pharmacist related factors. The content validity test of the questionnaire was carried out by three experts in the field of antidiabetic medication. About sixty DM type 2 patients were selected from primary health care centers to test the validity and reliability of The DMAB-Q. The test results showed that the questionnaire was valid (r value for each item > 0.254; n = 60) and reliable with a Cronbach's Alpha value of 0.821. The DMAB-Q consists of 22 questions: questions 1–8 relate to medication related factors, questions 9–17 relate to patient related factors, and questions 18–22 relate to healthcare provider related factor. The assessment used a four-point Likert scale: never = 1 point, sometimes = 2 points, often = 3 points, and always = 4 points. The author obtained the DMAB-Q score by adding the scores of each statement. Thus, the total DMAB-Q score ranged from 22 to 88, where a lower DMAB-Q score indicated fewer barriers to diabetes mellitus medication

adherence. Barrier adherence is categorized into two groups, high and low barrier adherence. Respondents are classified as having high barrier adherence if their total DMAB-Q score exceeds the mean ± 1 SD of the total scores of all respondents.

5.5 Statistical analysis

All data analyses were performed with statistical package for social science (SPSS version 20.0, Chicago, IL, USA). Descriptive analysis was used to assess the participants' demographic characteristics and examine each barrier factor related to adherence to antidiabetic medication. Cross-tabulation was performed to determine the frequency of patients with low and high barrier adherence using the DMAB questionnaire among demographic groups. Chi-square was conducted to investigate the association between patients' demographics and barriers to adherence to diabetes mellitus medication.

5.6 Ethical approval

The study was approved by The Ethical Committee of Medical Research, Medical Faculty, University of Lambung Mangkurat Banjarmasin, Indonesia (No.119/KEPK-FK ULM/EC/IV/2022). Permission was granted by the heads of the primary healthcare centers. Formal consent is obtained from the participants. Participants were assured of confidentiality and anonymity of their responses.

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REFERENCES

[1] ElSayed NA, Aleppo G, Aroda VR, Bannuru RR, Brown FM, Bruemmer D, Collins BS, Gaglia JL, Hilliard ME, Isaacs D, Johnson EL, Kahan S, Khunti K, Leon J, Lyons SK, Perry ML, Prahalad P, Pratley RE, Seley JJ, Stanton RC, Gabbay RA. .2. Classification and Diagnosis of Diabetes: Standards of Care in Diabetes-2023. Diabetes Care. 2023;46:19-40. https://doi.org/10.2337/dc23-S002

[2] Ojo OA, Ibrahim HS, Rotimi DE, Ogunlakin AD, Ojo AB. Diabetes mellitus: From molecular mechanism to pathophysiology and pharmacology. Med Nov Technol Devices. 2023;19:247-255. https://doi.org/10.1016/j.medntd.2023.100247

[3] Alshahrani JA, Alshahrani AS, Alshahrani AM, Alshalaan AM, Alhumam MN, Alshahrani NZt. The Impact of Diabetes Mellitus Duration and Complications on Health-Related Quality of Life Among Type 2 Diabetic Patients in Khamis Mushit City, Saudi Arabia. Cureus. 2023;15(8):e44216. https://doi.org/10.7759/cureus.44216

[4] Tomic D, Shaw JE, Magliano DJ. The burden and risks of emerging complications of diabetes mellitus. Nat Rev Endocrinol. 2022;18:525-539. https://doi.org/10.1038/s41574-022-00690-7

[5] Leon BM, Maddox TM. Diabetes and cardiovascular disease: Epidemiology, biological mechanisms, treatment recommendations and future research. World J Diabetes. 2015;6:1246-1258. https://doi.org/10.4239/wjd.v6.i13.1246

[6] Animaw W, Seyoum Y. Increasing prevalence of diabetes mellitus in a developing country and its related factors. PLoS One. 2017;12(11):e0187670.https://doi.org/10.1371/journal.pone.0187670

[7] Khan MAB, Hashim MJ, King JK, Govender RD, Mustafa H, Al Kaabi J. Epidemiology of Type 2 Diabetes - Global burden of disease and forecasted trends. J Epidemiol Glob Health. 2020;10:107-111. https://doi.org/10.2991/jegh.k.191028.001

[8] GBD 2021 Diabetes Collaborators. Global, regional, and national burden of diabetes from 1990 to 2021, with projections of prevalence to 2050: a systematic analysis for the Global Burden of Disease Study 2021. Lancet. 2023;402(10397):203-234. doi:10.1016/S0140-6736(23)01301-6. Erratum in: Lancet. 2023;402(10408):1132. doi: 10.1016/S0140-6736(23)02044-5. Erratum in: Lancet. 2025;405(10474):202. https://doi.org/10.1016/S0140-6736(23)01301-6

[9] Wahidin M, Achadi A, Besral B, Kosen S, Nadjib M, Nurwahyuni A, Ronoatmodjo S, Rahajeng E, Pane M, Kusuma D. Projection of diabetes morbidity and mortality till 2045 in Indonesia based on risk factors and NCD prevention and control programs. Sci Rep. 2024;14:5424-5441. https://doi.org/10.1038/s41598-024-54563-2

[10] Soeatmadji DW, Rosandi R, Saraswati MR, Sibarani RP, Tarigan WO. Clinicodemographic Profile and Outcomes of Type 2 Diabetes Mellitus in the Indonesian Cohort of DISCOVER: A 3-Year Prospective Cohort Study. J ASEAN Fed Endocr Soc. 2023;38:68-74. https://doi.org/10.15605/jafes.038.01.10

[11] Sankar V, Justin A, Matin PH, Pradeep S, Charan Kumar NS. Medication adherence and clinical outcomes in type 2 diabetes mellitus patients with depression: a prospective interventional study. J Res Pharm. 2018;22:269-276. https://doi.org/10.12991/jrp.2018.102
[12] Presley B, Groot W, Pavlova M. Pharmacy-led interventions to improve medication adherence among adults with diabetes: A systematic review and meta-analysis. Res Social Adm Pharm. 2019;15:1057-1067. https://doi.org/10.1016/j.sapharm.2018.09.021
[13] Yilmaz Z, Bulut K. Necessity and impact of patient education driven by pharmacist on the knowledge level of diabetic patients. J Res Pharm. 2023;27:1911-1923. https://doi.org/10.29228/jrp.473
[14] Liu H, Yao Z, Shi S, Zheng F, Li X, Zhong Z. The Mediating effect of self-efficacy on the relationship between medication literacy and medication adherence among patients with Type 2 Diabetes. Patient Prefer Adherence. 2023;17:1657-1670. https://doi.org/10.2147/PPA.S413385
[15] Alsaidan AA, Alotaibi SF, Thirunavukkarasu A, BF AL, Alharbi RH, Arnous MM, Alsaidan OA, Alduraywish AS, Alwushayh YA. Medication adherence and its associated factors among patients with Type 2 Diabetes Mellitus attending primary health centers of eastern province, Saudi Arabia. Medicina (Kaunas). 2023;59(5):989. https://doi.org/10.3390/medicina59050989
[16] Panahi S, Rathi N, Hurley J, Sundrud J, Lucero M, Kamimura A. Patient Adherence to Health Care Provider Recommendations and Medication among Free Clinic Patients. J Patient Exp. 2022;9:23743735221077523. https://doi.org/10.1177/23743735221077523
[17] Bombard Y, Baker GR, Orlando E, Fancott C, Bhatia P, Casalino S, Onate K, Denis JL, Pomey MP. Engaging patients to improve quality of care: a systematic review. Implement Sci. 2018 ;13(1):98. https://doi.org/10.1186/s13012-018-0784-z
[18] Krass I, Schieback P, Dhippayom T. Adherence to diabetes medication: a systematic review. Diabet Med. 2015;32:725-737. https://doi.org/10.1111/dme.12651
[19] Khunti K, Seidu S, Kunutsor S, Davies M. Association between adherence to pharmacotherapy and outcomes in Type 2 Diabetes: A Meta-analysis. Diabetes Care. 2017;40:1588-1596. https://doi.org/10.2337/dc16-1925
[20] Piragine E, Petri D, Martelli A, Calderone V, Lucenteforte E. Adherence to oral antidiabetic drugs in patients with Type 2 Diabetes: Systematic review and meta-analysis. J Clin Med. 2023;12:1981-2004. https://doi.org/10.3390/jcm12051981
[21] Kvarnstrom K, Westerholm A, Airaksinen M, Liira H. Factors contributing to medication adherence in patients with a chronic condition: A scoping review of qualitative research. Pharmaceutics. 2021;13:1100-1141. https://doi.org/10.3390/pharmaceutics13071100
[22] Kardas P. From non-adherence to adherence: Can innovative solutions resolve a longstanding problem? Eur J Intern Med. 2024;119:6-12. https://doi.org/10.1016/j.ejim.2023.10.012
[23] Pertiwi MV, Alfian R, Nita Y, Athiyah U. Medication adherence of diabetes mellitus patients in Indonesia: A systematic review. Pharm Edu. 2022;2:188-193. https://doi.org/10.46542/pe.2022.222.188193
[24] Kao CC, Hsieh HM, Lee DY, Hsieh KP, Sheu SJ. Importance of medication adherence in treatment needed diabetic retinopathy. Sci Rep. 2021;11:1910-1918. https://doi.org/10.1038/s41598-021-98488-6
[25] Faisal K, Tusiimire J, Yadesa TM. Prevalence and factors associated with non-adherence to antidiabetic medication among patients at Mbarara Regional Referral Hospital, Mbarara, Uganda. Patient Prefer Adherence. 2022;16:479-491. https://doi.org/10.2147/PPA.S343736
[26] Araya EM, Gebrezgabiher HA, Tekulu GH, Alema NM, Getnet D, Gebru HT, Adamu BA. Medication non-adherence and associated factors among diabetic patients visiting general hospitals in the eastern zone of Tigrai, Northern Ethiopia. Patient Prefer Adherence. 2020;14:2071-2083. https://doi.org/10.2147/PPA.S278148
[27] Rezaei M, Valiee S, Tahan M, Ebtekar F, Ghanei Gheshlagh R. Barriers of medication adherence in patients with type-2 diabetes: a pilot qualitative study. Diabetes Metab Syndr Obes. 2019;12:589-599. https://doi.org/10.2147/DMSO.S197159
[28] Nelson LA, Wallston KA, Kripalani S, LeStourgeon LM, Williamson SE, Mayberry LS. Assessing barriers to diabetes medication adherence using the Information-Motivation-Behavioral skills model. Diabetes Res Clin Pract. 2018;142:374-384. https://doi.org/10.1016/j.diabres.2018.05.046
[29] Huang YM, Shiyanbola OO. Investigation of barriers and facilitators to medication adherence in patients with Type 2 Diabetes across different health literacy levels: An explanatory sequential mixed methods study. Front Pharmacol. 2021;12:745749. https://doi.org/10.3389/fphar.2021.745749
[30] Muller S, Kohlmann T, Wilke T. Validation of the adherence barriers questionnaire - an instrument for identifying potential risk factors associated with medication-related non-adherence. BMC Health Serv Res. 2015;15:153-165. https://doi.org/10.1186/s12913-015-0809-0
[31] Hatah E, Rahim N, Makmor-Bakry M, Mohamed Shah N, Mohamad N, Ahmad M, Haron NH, Sze Hwe C, Tan Meng Wah A, Hassan F, Shaik Rahmat S, Robert SA, Abdullah N. Development and validation of Malaysia Medication Adherence Assessment Tool (MyMAAT) for diabetic patients. PLoS One. 2020;15(11):e0241909. https://doi.org/10.1371/journal.pone.0241909
[32] Atinga RA, Yarney L, Gavu NM. Factors influencing long-term medication non-adherence among diabetes and hypertensive patients in Ghana: A qualitative investigation. PLoS One. 2018;13(3):e0193995.https://doi.org/10.1371/journal.pone.0193995

[33] Rosendal M, Carlsen AH, Rask MT, Moth G. Symptoms as the main problem in primary care: A cross-sectional study of frequency and characteristics. Scand J Prim Health Care. 2015;33:91-99. https://doi.org/10.3109/02813432.2015.1030166
[34] Telo GH, de Souza MS, Andrade TS, Schaan BD. Comparison between adherence assessments and blood glucose monitoring measures to predict glycemic control in adults with type 1 diabetes: a cross-sectional study. Diabetol Metab Syndr. 2016;8:54-60. https://doi.org/10.1186/s13098-016-0162-4
[35] Sendekie AK, Netere AK, Kasahun AE, Belachew EA. Medication adherence and its impact on glycemic control in type 2 diabetes mellitus patients with comorbidity: A multicenter cross-sectional study in Northwest Ethiopia. PLoS One. 2022;17(9):e0274971. https://doi.org/10.1371/journal.pone.0274971
[36] Suprapti B, Izzah Z, Anjani AG, Andarsari MR, Nilamsari WP, Nugroho CW. Prevalence of medication adherence and glycemic control among patients with type 2 diabetes and influencing factors: A cross-sectional study. Glob Epidemiol. 2023;5:100113. https://doi.org/10.1016/j.gloepi.2023.100113
[37] Lin LK, Sun Y, Heng BH, Chew DEK, Chong PN. Medication adherence and glycemic control among newly diagnosed diabetes patients. BMJ Open Diabetes Res Care. 2017 ;5(1):e000429. https://doi.org/10.1136/bmjdrc-2017-000429
[38] Alodhaib G, Alhusaynan I, Mirza A, Almogbel Y. Qualitative exploration of barriers to medication adherence among patients with uncontrolled Diabetes in Saudi Arabia. Pharmacy (Basel). 2021;9(1):16. https://doi.org/10.3390/pharmacy9010016
[39] Jaam M, Hadi MA, Kheir N, Mohamed Ibrahim MI, Diab MI, Al-Abdulla SA, Awaisu A. A qualitative exploration of barriers to medication adherence among patients with uncontrolled diabetes in Qatar: integrating perspectives of patients and health care providers. Patient Prefer Adherence. 2018;12:2205-2216. http://dx.doi.org/10.2147/PPA.S174652
[40] Jaam M, Mohamed Ibrahim MI, Kheir N, Hadi MA, Diab MI, Awaisu A. Assessing prevalence of and barriers to medication adherence in patients with uncontrolled diabetes attending primary healthcare clinics in Qatar. Prim Care Diabetes. 2018;12:116-125. https://doi.org/10.1016/j.pcd.2017.11.001
[41] Krzeminska S, Lomper K, Chudiak A, Ausili D, Uchmanowicz I. The association of the level of self-care on adherence to treatment in patients diagnosed with type 2 diabetes. Acta Diabetol. 2021;58:437-445. https://doi.org/10.1007/s00592-020-01628-z
[42] Bukhsh A, Goh BH, Zimbudzi E, Lo C, Zoungas S, Chan KG, Khan TM. Type 2 Diabetes Patients' Perspectives, Experiences, and Barriers Toward Diabetes-Related Self-Care: A Qualitative Study From Pakistan. Front Endocrinol (Lausanne). 2020;11:534873. https://doi.org/10.3389/fendo.2020.534873
[43] Polonsky WH, Henry RR. Poor medication adherence in type 2 diabetes: recognizing the scope of the problem and its key contributors. Patient Prefer Adherence. 2016;10:1299-1307. https://doi.org/10.2147/PPA.S106821
[44] Roborel de Climens A, Pain E, Boss A, Shaunik A. Understanding Reasons for treatment discontinuation, attitudes and education needs among people who discontinue Type 2 Diabetes treatment: Results from an online patient survey in the USA and UK. Diabetes Ther. 2020;11:1873-1881. https://doi.org/10.1007/s13300-020-00843-9
[45] Kassavou A, Sutton S. Reasons for non-adherence to cardiometabolic medications, and acceptability of an interactive voice response intervention in patients with hypertension and type 2 diabetes in primary care: a qualitative study. BMJ Open. 2017;7(8):e015597.https://doi.org/10.1136/bmjopen-2018-024121
[46] Walz L, Pettersson B, Rosenqvist U, Deleskog A, Journath G, Wandell P. Impact of symptomatic hypoglycemia on medication adherence, patient satisfaction with treatment, and glycemic control in patients with type 2 diabetes. Patient Prefer Adherence. 2014;8:593-601. https://doi.org/10.2147/PPA.S58781
[47] Lopez JM, Annunziata K, Bailey RA, Rupnow MF, Morisky DE. Impact of hypoglycemia on patients with type 2 diabetes mellitus and their quality of life, work productivity, and medication adherence. Patient Prefer Adherence. 2014;8:683-692. http://dx.doi.org/10.2147/PPA.S58813
[48] de Vries ST, Keers JC, Visser R, de Zeeuw D, Haaijer-Ruskamp FM, Voorham J, Denig P. Medication beliefs, treatment complexity, and non-adherence to different drug classes in patients with type 2 diabetes. J Psychosom Res. 2014;76:134-138. http://dx.doi.org/10.1016/j.jpsychores.2013.11.003
[49] Zor M, Bayer N, Gölbaşi Z. Analysis of the relationship between the use of traditional and complementary medical practices and health literacy levels in individuals with type II diabetes mellitus. J Res Pharm. 2021;25(5):756-764. https://doi.org/10.29228/jrp.67
[50] Aljofan M, Oshibayeva A, Moldaliyev I, Saruarov Y, Maulenkul T, Gaipov A. The rate of medication nonadherence and influencing factors: A systematic Review. e-J Gen Med. 2023;20:1-11. https://doi.org/10.29333/ejgm/12946
[51] Decroli E, Kam A, Dillasamola D. The Percentage of Depressive Symptoms in Patients with Type 2 Diabetes Mellitus in M Djamil General Hospital Padang, Indonesia. J Res Pharm. 2019;23:292-297. https://doi.org/10.12991/jrp.2019.136
[52] Mansoor SM, Aslani P, Krass I. Pharmacists' attitudes and perceived barriers to provision of adherence support in Australia. Int J Clin Pharm. 2014;36:136-144. https://doi.org/10.1007/s11096-013-9840-6
[53] Deters MA, Laven A, Castejon A, Doucette WR, Ev LS, Krass I, Mehuys E, Obarcanin E, Schwender H, Laeer S. Effective interventions for diabetes patients by community pharmacists: A Meta-analysis of pharmaceutical care components. Ann Pharmacother. 2018;52:198-211. https://doi.org/10.1177/1060028017733272

[54] Jeong S, Lee M, Ji E. Effect of pharmaceutical care interventions on glycemic control in patients with diabetes: a systematic review and meta-analysis. Ther Clin Risk Manag. 2018;14:1813-1829. https://doi.org/10.2147/TCRM.S169748

[55] Marjadi B, Alfian R, Susanto Y, Tjandra L, Pratama ANW, Schneider C. Pharmacists' continuing professional development for non-communicable diseases management: A consensus study. Res Social Adm Pharm. 2022;18:3964-3973. https://doi.org/10.1016/j.sapharm.2022.07.002

[56] Al Assaf S, Zelko R, Hanko B. The Effect of Interventions Led by Community Pharmacists in Primary Care for Adults with Type 2 Diabetes Mellitus on Therapeutic Adherence and HbA1c Levels: A Systematic Review. Int J Environ Res Public Health. 2022;19(10):6188. https://doi.org/10.3390/ijerph19106188

[57] Alsairafi Z, Waheedi M, Alsaleh F. The perspectives of patients and physicians on the role of pharmacists in improving medication adherence in type 2 diabetes: a qualitative study. Patient Prefer Adherence. 2019;13:1527-1543. http://doi.org/10.2147/PPA.S218068

[58] Aditama L, Athiyah U, Utami W, Rahem A. Adherence behavior assessment of oral antidiabetic medication use: a study of patient decisions in long-term disease management in primary health care centers in Surabaya. J Basic Clin Physiol Pharmacol. 2020;30(6):/j/jbcpp.2019.30.issue-6/jbcpp-2019-0257/jbcpp-2019-0257.xml. https://doi.org/10.1515/jbcpp-2019-0257

[59] Iftinan GN, Elamin KM, Rahayu SA, Lestari K, Wathoni N. Application, benefits, and limitations of telepharmacy for patients with diabetes in the outpatient setting. J Multidiscip Healthc. 2023;16:451-459. https://doi.org/10.2147/JMDH.S400734

[60] Rabbani SA, Sharma S, Mahtab A, Pottoo FH, Sridhar SB. A systematic scoping review of implementation of telepharmacy during COVID-19. J Appl Pharm Sci. 2022;13:30-44. https://doi.org/10.7324/japs.2023.113646

[61] Alfian R, Athiyah U, Nita Y. Social media health interventions to improve diabetes mellitus patient outcome: a systematic review. J Basic Clin Physiol Pharmacol. 2021;32:297-304. https://doi.org/10.1515/jbcpp-2020-0501

[62] Gabarron E, Bradway M, Fernandez-Luque L, Chomutare T, Hansen AH, Wynn R, Arsaand E. Social media for health promotion in diabetes: study protocol for a participatory public health intervention design. BMC Health Serv Res. 2018;18:414-419. https://doi.org/10.1186/s12913-018-3178-7

[63] Onwuchuluba EE, Oyetunde OO, Soremekun RO. Medication Adherence in Type 2 Diabetes Mellitus: A Qualitative Exploration of Barriers and Facilitators From Socioecological Perspectives. J Patient Exp. 2021;8:23743735211034338. https://doi.org/10.1177/23743735211034338

[64] Xie Z, Liu K, Or C, Chen J, Yan M, Wang H. An examination of the socio-demographic correlates of patient adherence to self-management behaviors and the mediating roles of health attitudes and self-efficacy among patients with coexisting type 2 diabetes and hypertension. BMC Public Health. 2020;20:1227-1240. https://doi.org/10.1186/s12889-020-09274-4

[65] Davies MJ, Aroda VR, Collins BS, Gabbay RA, Green J, Maruthur NM, Rosas SE, Del Prato S, Mathieu C, Mingrone G, Rossing P, Tankova T, Tsapas A, Buse JB. Management of Hyperglycemia in Type 2 Diabetes, 2022. A Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetes Care. 2022;45:2753-2786. https://doi.org/10.2337/dci22-0034