Analysis of Patient Adherence to the Consumption of Single (Amlodipine) and Combination (Amlodipine + Captopril) Antihypertensive Medication through the Provision of Drug Information Services at the Kubang Jaya Community Health Center

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ARTICLE INFO	ABSTRACT
	The pharmacological treatment of hypertension is a multifaceted process that involves the use of antihypertensive medications to lower and control blood pressure. In previous studies, patient adherence has been reported to play an essential role in achieving successful medication outcomes and can be improved by providing Drug Information Services (DIS) to enhance the understanding of medication instructions. Therefore, this study aimed to assess the effect of providing DIS on patient adherence to the consumption of single (amlodipine) and combination (amlodipine + captopril) antihypertensive medication at the Technical Implementation Unit of the Kubang Jaya Community Health Center. A non-experimental approach with a cross-sectional design was used, and respondents who fulfilled the inclusion criteria were divided into the DIS and non-DIS groups. After a 10-day medication period, respondents were given questionnaires to assess their adherence to the consumption of amlodipine and amlodipine + captopril medication. Mann-Whitney analysis showed a p-value of 0.000 ($\alpha<0.05$), indicating the presence of a significant difference in adherence between the DIS and non-DIS groups. Based on the Chi-Square analysis results, a p-value of 0.000 ($\alpha<0.05$) was obtained, showing that sex, education, occupation, and age significantly affected the medication adherence in hypertensive patients. However, there was no significant difference in the effects of consuming amlodipine and amlodipine + captopril antihypertensive medications. The provision of clear and informative DIS had a positive effect on patient adherence to both amlodipine and amlodipine + captopril antihypertensive medications.

1. Introduction

Patient adherence to medication for hypertension is an essential aspect that play a crucial role in the management of condition [1]. Furthermore, several factors have been identified to influence the success of antihypertensive medication, including patient adherence [2].

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Non-adherence among affected individuals, specifically those at high risk, can lead to severe cardiovascular complications such as heart attacks, strokes, and kidney failure [3]. According to previous reports, hypertension is a cardiovascular disease characterized by elevated blood pressure, typically ≥ 120/80 mmHg. This condition is commonly referred to as the "silent disease" because patients are often unaware of its presence due to the absence of symptoms, complications, or death [4]. Pharmacological medications for hypertension include antihypertensive medication to lower and control blood pressure [5]. Affected patients who fail to adhere to their medication regimen often experience inadequate control of their condition [6]. Several studies have identified perceived side effects as a major cause of non-adherence, and in some cases, patients can discontinue medication [7]. The main reasons for low adherence to medication included forgetfulness, improvement in well-being, side effects, and running out of medications [8].

Various factors have been reported to contribute to inadequate blood pressure control in hypertension, including suboptimal adherence, failure to initiate pharmacotherapy, noncompliance with prescribed medication, and discontinuation of medication [1]. Hypertension management places strong emphasis on addressing medication adherence, as there has been no recent discovery of antihypertensive drugs. Therefore, compliance with regular drug consumption is a major factor for achieving medication success [9]. The most useful approaches to support adherence reported by participants were cheaper and single-pill combinations as well as leaflets providing better information on treatment. Information provided by physicians on hypertension and its treatment was considered sufficient for only 54% patient [8]. Improving patient adherence can be viewed from a more practical perspective, such as enhancing the patient-practitioner relationship as a key element and selecting interventions designed for each individual profile [10]. An effective method to enhance communication is through Drug Information Services (DIS), which foster two-way communication and interaction between practitioners and patients.

According to data from the Kampar Regency Health Department in 2021, hypertension is among the top 10 most prevalent diseases, with 14,662 reported cases. An essential aspect of adherence is understanding medication instructions. Improving the understanding of medication instructions and compliance is significantly affected by pharmaceutical service interventions, specifically the provision of DIS. Furthermore, DIS can change patient knowledge and adherence, pharmacists, and other healthcare professionals, as well as play a crucial role in effective communication to provide understanding and knowledge about drugs and diseases. A survey conducted at the Technical Implementation Unit of The Kubang Jaya Community Health Center showed that the number of patients with hypertension ranged from approximately 100 to 200 per month. The most commonly prescribed antihypertensive drugs in this setting include calcium channel blockers such as amlodipine and a combination of calcium channel blockers and ACE inhibitors such as amlodipine and captopril.

The Kubang Jaya Community Health Center is healthcare service in Kampar Regency, Riau, Indonesia, with the highest number of hypertensive patients. However, the provision of pharmaceutical services, including DIS, has not been optimal, primarily owing to a lack of understanding by healthcare professionals about the importance and barriers faced by patients. These barriers include difficulties in interpreting information, forgetfulness, fatigue, and a sense of cure, leading to diminished attention during DIS education.

2. Methodology

This study used a non-experimental cross-sectional method, and data were collected prospectively by examining the questionnaire responses from respondents at the Technical Implementation Unit of the Kubang Jaya Community Health Center. Furthermore, the adherence

level was measured, and DIS was provided before the procedures. The DIS provided includes the medication name, composition, indications, dose/administration instructions, side effects, storage, non-pharmacological recommendations, reminders to take medication regularly, instructions to take missed antihypertensive medication once remembered, and when the next dose time was near, patients were not to consume the missed dosage but returned to the regular schedule. The services also included displaying a supportive attitude and behavior, such as encouraging patients to ask questions about unclear information. After the provision of DIS, patients were administered a questionnaire to assess the effect of the intervention on adherence to the consumption of antihypertensive medication. This assessment was performed after 10 days of follow-up and prescription refilling.

The sample population in this study comprised 200 patients who were receiving and refilling prescriptions for a single (amlodipine) and combination (amlodipine + captopril) medication. The sampling method was based on the Slovin method, as follows:

$$n = \frac{N}{1+Ne^2} = \frac{200}{1+200(0.05)^2} = 57.14 = 58 \qquad (1)$$

where, N= number of samples, *n* = total population = 200 and e = error tolerance limit = 0.05

Respondents were selected based on several inclusion criteria, including patients with a history of hypertension who were not pregnant and willing to participate, adults aged 20 years or older, and individuals receiving amlodipine and amlodipine + captopril. Data collection was performed by providing questionnaires that included patient characteristics and adherence to the consumption of antihypertensive medication through a modified MMAS-8. Furthermore, an explanation was provided regarding the completion methods, followed by collection and assessment for completeness. The study instruments were administered to the respondents twice, both before (pre) and after (post) the intervention.

The collected data were then subjected to Mann-Whitney and chi-square tests, and the p-value was compared to a significance level (α) of 5% or 0.05. When the p-value in the Mann-Whitney test was <0.05, there was a significant difference between the DIS and non-DIS groups. Meanwhile, when the p-value in the chi-square test was <0.05, the null hypothesis (H0) was rejected and the alternative hypothesis (H1) was accepted. Based on the results, there was a significant relationship between the independent variable (DIS) and the dependent variable (patient adherence to the consumption of antihypertensive medication). The proposed hypotheses are as follows:

H0: There is no effect of DIS on the adherence of hypertensive patients.
H1: There is an effect of DIS on the adherence of hypertensive patients.

3. Results
3.1 Patient Characteristics

This study was conducted at the Technical Implementation Unit of the Kubang Jaya Community Health Centre. In Table 1 patient characteristics included sex, education, occupation, and age.

Table 1

Distribution of patient characteristics in the Kubang Jaya Community Health Center Technical Implementation Unit

Patient characteristics		Treatment groups			
		DIS		Non-DIS	
		N	Percent (%)	N	Percent (%)
Gender	Male	7	24	11	38
	Female	22	76	18	62
Education	Undergraduate program	5	17	8	28
	Elementary school	12	41	5	17
	Senior high school	7	24	7	24
	Junior high school	5	17	9	31
Occupation	Housewives	5	17	14	48
	Others	9	31	5	17
	Private employees	6	21	1	3
	Civil servants	1	3	2	7
	Entrepreneurs	8	28	7	24
Age	< 43 years	14	48	9	31
	43 - 55 years	10	34	17	59
	> 55 years	5	17	3	10
Total		29	100	29	100

The analysis results showed that the majority of respondents were female, comprising 76% and 62% of the individuals in the DIS and non-DIS groups, respectively. In terms of education, most of respondents in the DIS and non-DIS groups had Elementary School education (41%) and Senior High School (24%), respectively. Furthermore, the majority of respondents in the DIS groups had other occupations (31%), while housewives represented the majority in the non-DIS group (48%). Based on age, most respondents in the DIS and non-DIS groups were below 43 years (48%) and between 43 and 55 years (59%), respectively.

3.2 Validity and Reliability

The validity test results are presented in Table 2. Questionnaires were used as measuring tools and tested for validity and reliability. The test was conducted by examining the questionnaire results, where a significance value (sig) < 0.05 was considered valid.

Table 2

Adherence questionnaire validity test results

Question	Pearson correlation	Sig	Description
K1	.644**	.000	Valid
K2	.783**	.000	Valid
K3	.583**	.000	Valid
K4	.770**	.000	Valid
K5	.657**	.000	Valid
K6	.521**	.000	Valid
K7	.583**	.000	Valid
K8	.525**	.000	Valid

Questionnaires were distributed to 58 respondents, and the results showed that the significance value (sig) was less than 0.05, indicating that all statement items were valid for the study. Furthermore, Cronbach's Alpha was > 0.6, specifically 0.792, indicating that all statement items were considered reliable or measurable, as shown in Table 3.

Table 3

Adherence questionnaire reliability test results

Reliability Statistics	
Cronbach's Alpha	N of Items
.792	8

3.3 Normality Test

Based on the obtained data in Table 4, it was concluded that all statement items were considered reliable. In this study, a normality test was conducted using the Kolmogorov-Smirnov test.

Table 4

Adherence normality test results

One-Sample Kolmogorov-Smirnov Test		
Descriptives		Percentage of adherence
N		58
Normal Parameters[a,b]	Mean	77.48
	Std. Deviation	26.329
Most Extreme Differences	Absolute	.321
	Positive	.196
	Negative	-.321
Test Statistic		.321
Asymp. Sig. (2-tailed)		.000[c]

a. Test distribution is Normal
b. Calculated from data
c. Lilliefors Significance Correction

The Kolmogorov-Smirnov test showed a significance value <0.05, and it was concluded that the data were not normally distributed.

3.4 Relationship between Patient Characteristics and Adherence

Based on Table 5, it was concluded that gender, education, occupation, and adherence to medication affected patient adherence levels.

Table 5

Analysis of the relationship between patient characteristics and adherence

Patient Characteristics		Groups		Chi Square
		Not adhere (score 0-4)	Adhere (score 5-8)	
Gender	Male	10	8	0.007
	Female	8	32	
Total		18	40	
Education	Undergraduate program	8	5	0.013
	Elementary school	1	16	
	Senior high school	5	9	
	Junior high school	4	10	
Total		18	40	
Occupation	Housewives	10	9	0.012
	Others	1	13	
	Private employees	0	7	
	Civil servants	2	1	
	Entrepreneurs	5	10	
Total		18	40	
Age	< 43 years	4	19	0.031
	43 - 55 years	13	14	
	> 55 years	1	7	
Total		18	40	

3.5 The Effect of DIS on Adherence

Based on Table 6 present medication adherence levels in both group in Table 7, there are the results of the chi square test.

Table 6

Adherence level result

		Groups		Total
		DIS	Non-DIS	
Adherence	Not adhere	0	18	18
	Adhere	29	11	40
Total		29	29	58

Table 7 shows a significance value of < 0.05, implying that the provision of DIS significantly affected medication adherence in both groups. Based on the Mann-Whitney test results with a p-value of 0.000 (< α = 0.05), there was a significant difference in adherence between the groups. Chi-square test results showed that the provision of DIS had a significant effect on medication adherence. The p-value 0.000 (< α = 0.05), leading to the rejection of H0 and acceptance of H1.

Table 7

Adherence level result

Data analysis	Chi-Square
The effect of DIS on adherence	0.000

3.6 The Effect of Single (Amlodipine) and Combination (Amlodipine + Captopril) Medication on Adherence

To determine the differences in adherence levels between patients receiving amlodipine and amlodipine + captopril medication, non-parametric tests were conducted using Mann-Whitney and Chi-Square tests. The Mann-Whitney test was used because the data were not normally distributed, and the results are presented in Tables 8 and 9.

Table 8

Mann-Whitney test results for DIS

Test Statistics[a]	
	Adherence
Mann-Whitney U	46.500
Wilcoxon W	481.500
Z	-6.288
Asymp. Sig. (2-tailed)	.000

a. Grouping Variable: DIS

Table 9

Mean rank results of Mann-Whitney test for patient medication

Ranks				
	Medication	N	Mean Rank	Sum of Ranks
Adherence	Amlodipine	13	14.88	193.50
	Amlodipine + Captoril	16	15.09	241.50
	Total	29		

4. Discussion

Research regarding the influence of drug information services on the level of patient adherence to taking medication at the UPT Puskesman Kubang Jaya was conducted with a total population of 200 patients and 58 samples who met the inclusion criteria. The sample of 58 people was divided into two groups the group with DIS as many as 29 people, and the group without DIS as many as 29 people. Before the results were analyzed, the validity and reliability of the questionnaire were tested. The results show that the questionnaire used is valid and reliable, as indicated by the Pearson correlation p-value, which is 0.00 for all questionnaire items, and the Cronbach's alpha value > 0.6, which is 0.792, indicating that all statements contained in the questionnaire are said to be reliable or reliable.

Most hypertensive patients at the Kubang Jaya Community Health Center receive single doses and combination doses; the single dose drug commonly used is the CCB group (amlodipine), the most widely used combination drug is a combination of CCB and ACE Inhibitor (amlodipine + captopril), which was obtained from survey results from 100% of the population where 80% received amlodipine and 20% received a combination (amlodipine and captopril). This drug is widely used in community health centers because it is a mandatory medication for community health centers. This drug was chosen because it has few side effects in accordance with Questionnaire Question 7 regarding comfort with perceived side effects; 81.03% of respondents stated that they did not feel any discomfort, while the remaining 18.97% stated that there were uncomfortable side effects, so it was wrong. A factor supporting medication adherence. This study also examined the influence of gender, age, education, and occupation on medication adherence. The levels of compliance and

noncompliance were measured using the total score. If the score is in the range of 0-4 then it is in the non-compliant category, whereas the score in the range of 5-8 is in the compliant category.

4.1 The Relationship between Gender and Adherence

In the gender group, the number of women was greater than that of men, as shown in Table 1. The effect of sex on adherence was analyzed using the chi-square test, leading to an Asymp. sig (2-sided) value. Based on the Chi-Square test results, the Pearson Chi-Square value was 0.007, which was less than $\alpha = 0.050$. Therefore, H0 was rejected and H1 was accepted, indicating the presence of a significant effect of gender on adherence. This is in line with research by Tambuwun, Suling, and Mintjelungan, which states that there is a significant relationship between gender and compliance with treatment for hypertension sufferers [11]. However, in other studies men were found to have a higher adherence to antihypertensive therapy than woman [12]

4.2 The Relationship between Age and Adherence

Age could be associated with medication adherence because, as individuals grow older, they tend to accumulate more knowledge, which affects thought patterns [13,14]. Based on the research results, the group that was given PIO was in the age range of< 43 years, namely 14 people (48%), and the group that was not given PIO was mostly in the age range of 43-55 years, namely 17 people (59%). The chi-square test results showed a significance value of 0.031, implying a significant effect of age on adherence. Which was consistent with Tambuwun, Suling, and Mintjelungan, who also found a significant relationship between the variables among hypertensive patients [11].

4.3 The Relationship between Education and Adherence

Based on the results of the research, looking at the level of education, the group that was given the PIO mostly had an elementary school education level, namely 12 people (41%), and the group that did not have a PIO had the highest school education level, namely 7 people (24%). The chi-squared test results showed a significance value of 0.013, implying that education had a significant effect on adherence. This was consistent with Ramadhani, who also reported similar results, stating that the level of education also greatly influences a person's compliance [13].

4.4 The Relationship between Occupation and Adherence

Occupation was related to health behaviors, such as adherence to the consumption of antihypertensive medication. This relationship was affected by the availability of free time, where working individuals tended to have limited time for healthcare appointments [13]. Based on the research results, the group who were given PIO were mostly patients who had other professions (casual workers, farmers, craftsmen, small traders), totaling 9 people (31%), and the group who did not have PIO mostly worked as housewives, totaling 14 people (48%). Furthermore, the chi-squared test results showed a significance value of 0.012, implying that occupation had a significant effect on adherence. This was in line with Listiana et al who also found a significant relationship between both variables among hypertensive patients being treated with medication [15].

Many factors can influence a person's compliance with pharmacological treatment, particulary the use of antihypertensive drugs. In other research, it was stated that the factors were age over 45 years, having knowledge of the disease, compliance with therapy, high level of self-efficacy, and/or

recognition of low levels of barriers. Meanwhile, factors that influence non-compliance with pharmacology treatment are age less than 35 years, difficulty in accessing a health center, in adequate follow-up of the disease, prescription of more than two antihypertensive drugs, diagnosis of hypertension less than five years, lack of knowledge of the disease, not trusting in the treatment or using alternative, complimentary, or traditional medicine [16].

4.5 The Effect of DIS on Adherence

This study focused on the effect of the DIS on patient adherence in the Technical Implementation Unit of the Kubang Jaya Community Health Center, and the procedures were conducted in April 2023. The sample population consisted of 200 patients, and the respondents comprised 58 individuals who fulfilled the inclusion and exclusion criteria. Subsequently, these individuals were equally divided into the DIS and non-DIS groups.

Statistical tests for research use the non-parametric test with two tests, namely, the Mann-Whitney test and the chi-square test. The Mann-Whitney U test was performed because the data were not normally distributed. Based on the results of the Mann-Whitney T test showing a p-value of 0.000 (< α = 0.05), according to the basis for decision making in the Mann-Whitney test, it can be concluded that there is a significant difference beetwen the group that was given DIS and the group that was not given DIS. on the level of compliance with medication in patients at the Technical Implementation Unit of the Kubang Jaya Community Health Center. Chi-square test results showed that the provision of DIS had a significant effect on medication adherence. The p-value was 0.000 (< α = 0.05), leading to the rejection of H0 and acceptance of H1. This was in line with Wani, where the intervention also had a significant influence [17]. Furthermore, this was supported by Kurniapuri regarding the effect of providing antihypertensive medication information on patient adherence in the Umbulharjo I Yogyakarta Community Health Center during the November 2014 period, with a p-value of 0.040 [18]. Based on these results, it was concluded that the provision of antihypertensive medication information significantly affected adherence.

Patients have their own expectations for their health services, such as patients expecting to receive complete information about the drugs and treatments they are undergoing. Based on this research, the unmet expectations of patients will contribute to poor treatment management. Therefore this PIO strategy will certainly be a means of listening and communicating directly with patients so that they can build a general understanding and treatment management plan, strengthen patient confidence, and increase their ability to manage medication effectively [19].

4.6 The Effect of Single (Amlodipine) and Combination (Amlodipine + Captopril) Medication on Adherence

To determine the differences in compliance levels between patients receiving amlodipine and amlodipine + captopril treatment, non-parametric tests were performed using the Mann-Whitney and Chi-Square tests. The Mann-Whitney test was used because the data were not normally distributed, and the results are presented in Table 6.

Table 6 shows that the data regarding the type of medication received by the patients had a significance value greater than 0.05. This showed that there was no significant difference between providing amlodipine and amlodipine + captopril medication in terms of adherence. Table 7 shows that amlodipine + captopril had a higher value than amlodipine alone, but this difference was not significant.

The majority of patients (80%) received amlodipine, while 20% received amlodipine and captopril as mandatory medications at the community health center. Amlodipine was selected because its minimal side effects, as indicated by the responses to Questionnaire item 7 regarding the comfort related to perceived side effects. A total of 81.03% of the respondents reported the absence of discomfort, while the remaining 18.97% reported discomfort due to side effects. Furthermore, lowering blood pressure has been recommended by several international guidelines as an effective strategy for preventing target organ damage and reducing cardiovascular risk-related mortality [20].

To assess the effect of DIS on patient adherence to amlodipine and amlodipine + captopril, a Mann-Whitney test was conducted. Table 6 showed that at higher mean rank was obtained for amlodipine + captopril, but there was no significant difference in adherence between patients receiving the two medical regimens. In the other research was found that the patients who taking under three-drug Single Pill Combination exhibited more frequently a high adherence to antihypertensive treatment than those prescribed a three-drug two pill combination [21,22]. Improvement in adherence translates into an important clinical advantage because adherence is inversely related to the risk of cardiovascular outcomes and mortality in a variety of studies [23,24]. Simplifying the regimen will increase patient compliance, besides that nowadays the use of applications can also help patients manage their treatment schedule consistently [25].

5. Conclusions

In conclusion, sex, age, education, and occupation significantly affected patient adherence. Furthermore, selecting the right method to improve adherence was crucial, and the DIS was a form of pharmaceutical care that could be provided. According to the Mann-Whitney analysis, there was a significant difference in the adherence level between the DIS and non-DIS groups (p= 0.000). Chi-square analysis showed that the provision of DIS significantly affected the variable among patients (p= 0.000), but there was no significant difference between amlodipine and amlodipine + captopril medication.

References
[1] Burnier, Michel, and Brent M. Egan. "Adherence in hypertension: a review of prevalence, risk factors, impact, and management." *Circulation research* 124, no. 7 (2019): 1124-1140. https://doi.org/10.1161/CIRCRESAHA.118.313220

[2] Mangendai, Yulike, Sefti Rompas, and R. Hamel. "Faktor-faktor yang berhubungan dengan kepatuhan berobat pada pasien hipertensi di Puskesmas Ranotana Weru." *Jurnal Keperawatan UNSRAT* 5, no. 1 (2017): 109214.

[3] Muhlis, Muhammad, and Alissa Jihan Prameswari. "Kepatuhan Penggunaan Obat Pada Pasien Hipertensi Di Instalasi Rawat Jalan Salah Satu Rsud Di Wilayah Daerah Istimewa Yogyakarta." *Jurnal Insan Farmasi Indonesia* 3, no. 1 (2020): 104-113. https://doi.org/10.36387/jifi.v3i1.491

[4] Arifin, M. H. B. M., I. Wayan Weta, and N. L. K. A. Ratnawati. "Faktor-faktor yang berhubungan dengan kejadian hipertensi pada kelompok lanjut usia di wilayah kerja UPT Puskesmas Petang I Kabupaten Badung tahun 2016." *E-jurnal Medika* 5, no. 7 (2016): 2303-1395.

[5] Sarumaha, Erna Krisnawati, and Vivi Eulis Diana. "Faktor risiko kejadian hipertensi pada usia dewasa muda di UPTD Puskesmas Perawatan Plus Teluk dalam Kabupaten Nias Selatan." *Jurnal Kesehatan Global* 1, no. 2 (2018): 70-77. https://doi.org/10.33085/jkg.v1i2.3914

[6] Williams, Bryan, Giuseppe Mancia, Wilko Spiering, Enrico Agabiti Rosei, Michel Azizi, Michel Burnier, Denis Clement et al. "2018 Practice Guidelines for the management of arterial hypertension of the European Society of Cardiology

and the European Society of Hypertension." *Blood Pressure* 27, no. 6 (2018): 314-340. https://doi.org/10.1080/08037051.2018.1527177

[7] Usman, Yusnita. "Analisis Efek Samping Penggunaan Obat Hipertensi Captopril Pada Pasien Rsud Kabupaten Enrekang." *Jurnal Ilmiah Kesehatan Diagnosis* 5, no. 1 (2020): 28-32.

[8] Prejbisz, Aleksander, Piotr Dobrowolski, Michel Burnier, Michel Azizi, Veronique Cornelissen, Vitoria Cunha, Pankaj Gupta et al. "Patient's Perspectives on Treatment Adherence in Hypertension: Results of an Esh Survey in Poland." *Journal of Hypertension* 41, no. Suppl 3 (2023): e80. https://doi.org/10.1097/01.hjh.0000939524.33988.bc

[9] Purnawinadi, I. Gede, and Irene Jessica Lintang. "Hubungan dukungan keluarga dengan kepatuhan minum obat pasien hipertensi." *Jurnal Skolastik Keperawatan* 6, no. 1 (2020): 35-41. https://doi.org/10.31290/jkt.v6i2.1572

[10] Poulter, Neil R., Claudio Borghi, Gianfranco Parati, Atul Pathak, Diana Toli, Bryan Williams, and Roland E. Schmieder. "Medication adherence in hypertension." *Journal of hypertension* 38, no. 4 (2020): 579-587. https://doi.org/10.1097/HJH.0000000000002294

[11] Tambuwun, Priscilia GJ, Pieter L. Suling, and Christy N. Mintjelungan. "Gambaran Keluhan Di Rongga Mulut Pada Pengguna Obat Antihipertensi Di Poliklinik Penyakit Dalam Rumah Sakit Tingkat III Robert Wolter Mongisidi Manado." *e-GiGi* 3, no. 2 (2015). https://doi.org/10.35790/eg.3.2.2015.8761

[12] Radic, Josipa, Hana Dogas, Marijana Vuckovic, Ela Kolak, Andrea Gelemanovic, Dora Bucan Nenadic, and Mislav Radic. "Medication adherence and gender difference in hypertensive patients." *Journal of Hypertension* 41, no. Suppl 3 (2023): e314. https://doi.org/10.1097/01.hjh.0000942268.39639.01

[13] Ramadhani, NS. "Analisis Pengaruh Keterampilan Mengajar, Emosi Mahasiswa, Tekanan Akademik Dan Perceived Academic Control Terhadap Prestasi Akademik Mahasiswa Menggunakan Pendekatan Structural Equation Modeling (SEM)." *World Dev* 1, no. 1 (2018): 1-15.

[14] Mahdarsari, Mayanti, Hanny Handiyani, and Hening Pujasari. "Peningkatan keselamatan diri perawat melalui optimalisasi fungsi manajemen." *Jurnal keperawatan indonesia* 19, no. 3 (2016): 176-183. https://doi.org/10.7454/jki.v19i3.472

[15] Listiana, Devi, Saputra Effendi, and Yayan Eka Saputra. "Faktor-faktor yang berhubungan dengan kepatuhan penderita hipertensi dalam menjalani pengobatan di Puskesmas Karang Dapo Kabupaten Muratara." *Journal of Nursing and Public Health* 8, no. 1 (2020): 11-22. https://doi.org/10.37676/jnph.v8i1.1005

[16] Montealegre, Leslie, Eulalia Amador, Tammy Pulido, Carlos Cabrera, Alma Rivera, and Roberto Rebolledo. "Main Factors That Determine Adherence To Pharmacological Treatment In Hypertensive Patients. Systematic Review." *Journal of Hypertension* 40, no. Suppl 1 (2022): e308. https://doi.org/10.1097/01.hjh.0000838740.81890.19

[17] Wani, Elsayanti, and Catur Retno Lestari. "Gambaran Penggunaan Obat Antihipertensi Pada Pasien Hipertensi Lanjut Usia 60-70 Tahun di UPTD. Puskesmas Lamasi Timur." *Indonesian Journal of Biomedical Science and Health* 1, no. 1 (2021): 23-33.

[18] Kurniapuri, Aulia, and Woro Supadmi. "Pengaruh Pemberian Informasi Obat Antihipertensi Terhadap Kepatuhan Pasien Hipertensi di Puskesmas Umbulharjo I Yogyakarta Periode November 2014." *Majalah Farmaseutik* 11, no. 1 (2015): 268-274.

[19] Ekman, Inger, Axel Wolf, Victoria Vaughan Dickson, Hayden B. Bosworth, and Bradi B. Granger. "Unmet expectations of medications and care providers among patients with heart failure assessed to be poorly adherent: results from the Chronic Heart Failure Intervention to Improve Medication Adherence (CHIME) study." *European Journal of Cardiovascular Nursing* 16, no. 7 (2017): 646-654. https://doi.org/10.1177/1474515117707669

[20] Burnier, Michel. "Drug adherence in hypertension." *Pharmacological research* 125 (2017): 142-149. https://doi.org/10.1016/j.phrs.2017.08.015

[21] Rea, Federico, Gabriella Morabito, Laura Savaré, Atul Pathak, Giovanni Corrao, and Giuseppe Mancia. "Adherence and related cardiovascular outcomes to single pill vs. separate pill administration of antihypertensive triple-combination therapy." *Journal of Hypertension* 41, no. 9 (2023): 1466-1473. https://doi.org/10.1097/HJH.0000000000003497

[22] Rea, Federico, Gabriella Morabito, Laura Savare, Giovanni Corrao, and Giuseppe Mancia. "PS-P07-8: Treatment Strategies and Adherence to the Triple Combination of an Angiotensin-Converting Enzyme Inhibitor, A Calcium-Channel Blocker, And A Diuretic." *Journal of Hypertension* 41, no. Suppl 1 (2023): e424-e425. https://doi.org/10.1097/01.hjh.0000917184.97398.97

[23] Corrao, Giovanni, Andrea Parodi, Federica Nicotra, Antonella Zambon, Luca Merlino, Giancarlo Cesana, and Giuseppe Mancia. "Better compliance to antihypertensive medications reduces cardiovascular risk." *Journal of hypertension* 29, no. 3 (2011): 610-618. https://doi.org/10.1097/HJH.0b013e328342ca97

[24] Kim, Soyeun, Dong Wook Shin, Jae Moon Yun, Yunji Hwang, Sue K. Park, Young-Jin Ko, and BeLong Cho. "Medication adherence and the risk of cardiovascular mortality and hospitalization among patients with newly prescribed

antihypertensive medications." *Hypertension* 67, no. 3 (2016): 506-512. https://doi.org/10.1161/HYPERTENSIONAHA.115.06731

[25] Mochartini, Tri, Hurairoh, Achmad Fauzi, Ikhwan Rinaldi, Novita, Abdul Aziz Setiawan. "Use of the Android-Based Application "LEUMYLO TRACKER" to Monitor Treatment Adherence in Chronic Myelocytic Leukaemia Patients," *Journal of Advanced Research in Applied Sciences and Engineering Technology* 60, no. 1, (2024):219-231. https://doi.org/10.37934/araset.60.2.219231