JURNAL FARMASI SAINS DAN KOMUNITAS
Journal of Pharmaceutical Sciences & Community

p-ISSN 1693-5683; e-ISSN 2527-7146

Vol. 21, No. 2, November 2024, pp. 190-199

Research Article

The Effect of Adherence to Antihypertensive Therapy and Cardiovascular Risk Among Hypertensive Patients in Purworejo Regency

Prili Arwinda[1,2], Dita Maria Virginia[2], Phebe Hendra[2*]

[1]Wirun Kutoarjo Primary Health Care, Central Java 54212, Indonesia.
[2]Faculty of Pharmacy, University Sanata Dharma, Yogyakarta 55282, Indonesia.

https://doi.org/10.24071/jpsc.007334

J. Pharm. Sci. Community, 2024, 21(2), 190-199

Article Info

Received: 12-10-2023
Revised: 24-11-2023
Accepted: 28-11-2023

***Corresponding author:**
Phebe Hendra
email:
phebe_hendra@usd.ac.id

Keywords:
Adherence; Blood pressure; Cardiovascular risk; Medication adherence report scale-5; Medication possession ratio

ABSTRACT

Uncontrolled hypertension will increase mortality and morbidity rates. The adherence is an important factor in controlling blood pressure. Uncontrolled blood pressure will affect cardiovascular risk. Therefore, hypertensive patients must comply with taking medication to control blood pressure and cardiovascular risk. This study was an analytical observational study with a cross-sectional design. A total of 85 respondents who met the inclusion criteria were measured for adherence using the MPR (Medication Possession Ratio) method and the MARS-5 (Medication Adherence Report Scale-5) questionnaire. A patient who had blood pressure <140/90 mmHg was categorized as controlled hypertension. The cardiovascular risk was measured using the ACC/AHA criteria method. Data were analyzed using chi-square tests and odds ratio (OR) with 95% confidence interval (CI) and $p<0.05$ considered significant. This study showed that there was a significant association between adherence to antihypertensive therapy to controlled blood pressure, either according to MPR (OR=18.262; 95%CI=5.259-63.412; p=0.000) and MARS-5 (OR=31.607; 95%CI=8.170-122.277; p=0.000). A significant association was found between antihypertensive adherence and cardiovascular risk, either according to MPR (OR=3.733; 95%CI=1.269-10.983; p=0.020) and MARS-5 (OR=9.000; 95%CI=2.702-29.983; p=0.000). Therefore, this study concludes a significant relationship between antihypertensive adherence to controlled blood pressure and cardiovascular risk in Purworejo Regency.

INTRODUCTION

Non-communicable diseases (NCDs) are the leading cause of death globally. One of the non-communicable diseases that is becoming the most severe health problem today is hypertension. According to the World Health Organization (WHO) predictions, 1.5 billion individuals will have been diagnosed with hypertension by 2025 (WHO, 2020). Based on Basic Health Research in Indonesia, the prevalence of hypertension in the population over 18 years of age increased to 34.1% (Kemenkes RI, 2018).

Uncontrolled hypertension can increase the risk of mortality and morbidity rates. One of the most serious issues in the developing crisis is non-adherence to antihypertension medication, a condition or issue that is detectable and controllable. (Mebrahtu *et al*., 2021). The adherence of hypertensive patients can be measured using the Medication Adherence Report Scale-5 (MARS-5) method, an instrument to measure the level of adherence of chronic disease patients with five domain questions (Asseggaf and Ulfah, 2022; Chan *et al*., 2020; Wibowo *et al*., 2021). Another measurement is the Medication Possession Ratio (MPR), a

method that is often used and valid because it is reliable and objective in long-term drug use (Srikartika *et al*., 2016). Previous research has demonstrated a strong relationship between patient adherence and blood pressure control, with patient adherence having an impact on the patient's blood pressure reduction throughout therapy (Akri *et al*., 2022; Rahmadani and Sari, 2018).

Patients with hypertension have the risk of not adhering to treatment. Non-adherence in patients with hypertension can increase the number of cardiovascular risk events. Based on the Indonesian Hypertension Doctors Association, hypertensive patients have a cardiovascular risk of up to 50% (PDHI, 2021). The American College of Cardiology/American Heart Association (ACC/AHA) method is used to predict the level of atherosclerotic cardiovascular risk in the next ten years (PERKI, 2022), which can be used as a guide (Dwivani *et al.*, 2018). The ACC/AHA method is superior to other methods for preventing cardiovascular risk because it can better recommend statin therapy appropriately. According to the findings, using statins based on the ACC/AHA criteria as opposed to the European Society of Cardiology/European Atherosclerosis Society (ESC/EAS) criteria led to a significant improvement in sensitivity (+62% for any atherosclerotic cardiovascular diseases [ASCVD] and +76% for fatal ASCVD) and a slight decrease in specificity (-35% for any ASCVD and -36% for fatal ASCVD) (Mortensen *et al*., 2017). Based on this, cardiovascular risk detection is necessary as early as possible.

To control hypertension, various efforts have been made by the Indonesian Government to collaborate with the Health Social Security Organizing Agency (BPJS) in implementing the Chronic Disease Management Program (*Prolanis*) at First Level Facilities (FKTP). *Prolanis* is a health service system and proactive approach for BPJS Kesehatan participants who suffer from chronic diseases to achieve optimal quality of life with effective and efficient health service costs involving participants, BPJS and health facilities. Previous studies have shown that patients who take part in *Prolanis* activities can encourage patient independence, increase patient satisfaction with the treatment being carried out and can improve the quality of life of patients and control health service costs in the long term (Manninda *et al*., 2021).

Purworejo Regency is one of Central Java's regencies with a higher prevalence of hypertension than the national prevalence, reaching 36.6% (RISKESDAS, 2018). Based on data from the Purworejo District Health Service in 2021, it was reported that hypertension was ranked in the top two diseases most suffered by 41,693 people. The adherence factors are very influential in hypertensive patients. Several studies have shown the effect of adherence on its therapeutic outcome targets (Adisa *et al*., 2020; Shaleha *et al.*, 2019). However, some research indicates that there is no significant correlation between therapeutic outcome targets and adherence (Azmi *et al*., 2021). Therefore, this study was conducted to assess the impact of antihypertensive therapy adherence on regulated blood pressure and cardiovascular risk among patients with hypertension.

METHODS

The study was an analytical observational cross-sectional study that used a purposive sampling technique. The inclusion criteria were: *Prolanis* patients aged 40-70 years and had used antihypertensive therapy with at least 3 visits in 1 year in the period July 2022 to June 2023 in Purworejo Regency. The exclusion criteria were patients who used antihypertensive with non-cardiovascular indications, patients with comorbidities, and pregnant patients.

The study began with data collection of history among the *Prolanis* patients. We recruited 104 hypertensive patients (**Figure 1**). A total of 19 subjects were excluded because 8 patients were diagnosed with congestive heart failure (CHF), 6 patients were diagnosed with stroke, 1 patient was diagnosed with renal function abnormalities, and 4 patients were diagnosed with hypertensive heart disease (HHD).

Based on Hypertension Management Consensus 2019, the subject's blood pressure (BP) was categorized as controlled (BP <140/90 mmHg) and uncontrolled (systolic BP ≥140 or diastolic BP ≥90 mmHg). Assessment of the patient therapy adherence was based on the MARS-5 and MPR scores. Subjects with good adherence have an MPR value of >0.8 and subjects with less insufficient adherence have an MPR value of ≤0.8 (Kozma *et al*., 2013). The MARS-5 assessment score is divided into two categories: low adherence with a score <25 and high adherence with a score of 25 (Kane et al., 2008). Based on the ACC/AHA method, ASCVD risk is grouped into low-risk (<7.5%) and high-risk (>7.5%) fields (Anharudin and Tejamaya, 2022).

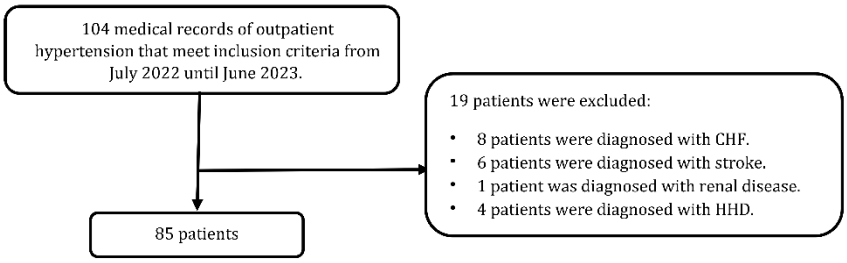


Figure 1. Flow diagram of the sampling process and subject criteria

Table 1. Characteristics of patients in the period July 2022 – June 2023.

Characteristics of patients	Patients (n = 85)	
	n	%
Gender		
Male	18	21.2
Female	67	78.8
Age		
40 - 59 years	37	43.5
60 -79 years	48	56.5
Education		
Low education	82	96.5
High education	3	3.5
Occupation		
Employed	47	55.3
Unemployed	38	44.7
Smoking Status		
Smoking	7	8.2
No Smoking	78	91.8
Hypertension therapy		
Monotherapy	63	74.2
Combination	22	25.8
Duration of Hypertension		
Less than 5 years	46	54.1
More than 5 years	39	45.9
Adherence Therapy (MARS-5)		
High Adherence	63	74.1
Low Adherence	22	25.9
Adherence Therapy (MPR)		
High Adherence	65	76.5
Low Adherence	20	23.5
Blood Pressure		
Controlled	66	77.6
Uncontrolled	19	22.4
ASCVD Risk		
Low Risk	46	54.1
High Risk	39	45.9

In this study, chi-square statistical tests were applied in univariate and bivariate data analysis. The Health Research Ethics Commission of the Respati University Yogyakarta has approved this study because it complies with its ethical standards (0188.3/FIKES/PL/VIII/2023)

RESULTS AND DISCUSSION

Table 1 shows the distribution of patient characteristics in the July 2022 - June 2023 period. In this study, the characteristics of patients with hypertension were primarily female patients (78.8%) at the age of over 60 years (56.5%) with non-smoking status (91.8%). The distribution of patient characteristics based on employment status found that the majority of patients (55.3%) had a working status while for the education level variable, it was found that 96.5% had a low level of education. Most respondents (54.1%) were known to have suffered from hypertension for less than 5 years and as many as (74.2%) of patients used a type of hypertension monotherapy. In the level of adherence to therapy of hypertensive patients with MPR measurements, it was found that there were 76.5% who were in the adherence category. While with MARS-5 questionnaire measurements, 74.1% of the patients with hypertension were in the adherence category. Table 1 shows that 54.1% had a low risk of ASCVD while 45.9% had a high risk of ASCVD.

Based on this research, it shows that women have a greater risk of hypertension. One factor that affects blood pressure is gender, especially in people over 65. The prevalence of hypertension in women was 22.8% (Kemenkes RI, 2018). Previous research showed that women had a risk of developing hypertension in 27.5% while for men it was only 5.8% (Wahyuni and Eksanoto, 2013). Women who are older than 45 will have a higher chance of developing high blood pressure after menopause. Estrogen protects women who have not yet reached menopause and contributes to the rise in High-Density Lipoprotein (HDL) levels. High low-density lipoprotein (LDL) cholesterol and low HDL cholesterol levels influence the development of atherosclerosis, which in turn causes high blood pressure (Hage *et al*., 2013). This study is consistent with that of a previous study (Livana and Basthomi, 2020), who conducted research in Kendal City and found that gender is related to and a risk factor for the prevalence of hypertension (p=0.000, r= 0.316).

The prevalence of hypertension is very high, reaching 60% to 80% of the older age population, and is particularly high in the elderly population over the age of 60. Data from the Basic Health Research results show that the prevalence of hypertension in Indonesia continues to increase in the elderly age group, namely at the age of 65-74 years by 63.2% and age over 75 years by 69.5% (Kemenkes RI, 2018). The age factor has a significant impact on the prevalence of hypertension because as people age, their chance of developing the condition increases. A person's blood pressure will rise along with their advancing age, which can be caused by several factors, such as natural changes in a person's heart and blood vessels. These changes occur naturally as part of the aging process. Age-related widening and stiffening of the body's arteries cause a reduction in the capacity and rebound of blood flowing through the blood vessels. The systole pressure rises because of this lowering. Additionally, aging interferes with neurohormonal systems including the renin-angiotensin-aldosterone system. Additionally, it results in elevated peripheral plasma concentrations, glomerulosclerosis brought on by age, and intestinal fibrosis, all of which increase vasoconstriction and vascular resistance and hence raise blood pressure (Maulidina, 2019). Table 1 shows that most of the patients with hypertension were reaching elderly ages.

In this study, education is related to the incidence of hypertension because more respondents have low education. Due to a lack of information or knowledge that results in harmful behavior and lifestyles, such as ignorance of the risks and methods for preventing the development of hypertension, low education raises the likelihood that a person may develop hypertension (Maulidina, 2019). These data are supported by the results of the Basic Health Research, which states that people with lower education levels tend to have greater rates of hypertension, which may be related to a lack of knowledge about a healthy diet (Kemenkes RI, 2018). Therefore, one of the aspects that can impact a person's comprehension of how to absorb information is their level of education (Taiso *et al*., 2021).

Table 1 also shows that work factors influence a person to develop hypertension. The prevalence of hypertension varies between occupational groups and is directly tied to the sort of job that is performed. People who have physically demanding jobs are more likely to acquire high blood pressure (Cheng *et al*., 2021). Lifting heavy weights causes a large and acute increase in blood pressure. This may be caused by vasoconstriction, which increases peripheral resistance, and thereby an increase in blood pressure. Another study revealed that office workers with long workdays were also at risk for high blood pressure. According to gender, both men's and women's occurrence of hypertension are significantly influenced by the longest workweeks (56 hours) (Clays *et al*., 2012).

The results showed that for smoking status, 78 respondents did not smoke. This is because the hypertensive patients in this study were predominately women. Smoking habits, however, can have an impact because they are a daily necessity for the individual and are the source of their elevated blood pressure. Because nicotine and tar compounds can destroy the lining of arterial blood vessel walls and result in the development of atherosclerosis and hypertension, smoking will result in an accumulation of dangerous substances in the blood that can lead to a variety of cardiovascular problems (Erman *et al*., 2021).

The level of adherence to therapy in most patients in this study was in the monotherapy group. Monotherapy drugs were given more frequently for the treatment of hypertensive patients with a percentage of 50.7%, while combination therapy was only given at 49.3% (Akri *et al*., 2022). The most widely used antihypertensive drug used by geriatric patients undergoing treatment is monotherapy. The use of monotherapy is known to increase patient adherence with using medication. Patients who receive combination drugs will tend to have low adherence in taking medication (Runtuwene *et al*., 2019). The more medication items that are received and must be consumed in a day can reduce the level of patient adherence. Another reason that can cause non-adherence is that patients feel they are experiencing side effects (Pratidina *et al*., 2021).

The findings of this study demonstrate that patients with hypertension who have had their condition for fewer than five years had higher levels of drug adherence. According to the WHO, adherence with taking medication for hypertension sufferers in Indonesia who have experienced hypertension for 1-5 years tend to be more compliant with the process of taking medication, while patients who have experienced hypertension for 6-10 years tend to have poorer adherence with taking medication due to the long-term factor suffering, work, bored of taking medication, lack of support from family, have insufficient adherence and non-adherence (WHO, 2010). The duration of suffering from hypertension for less than five years is higher than that for more than five years (68.9%) (Liberty *et al*., 2018). It has been reported that a person's degree of adherence decreases with the length of time they have been affected by hypertension. This is because the majority of patients will grow weary of receiving therapy, and the longer a person has hypertension, the more probable it is that they will disobey instructions because they will grow weary of receiving care or taking medication, even though the recovery rate is not as anticipated (Gama *et al*., 2014).

In this study, to measure adherence, a combination of two measurements was used, namely subjective measurement using the MARS-5 questionnaire and objective measurement using the MPR calculation method. This approach is because the use of the questionnaire method has a tendency for patients to refrain from reporting non-adherence. Therefore, objective measurements must be used to validate and correlate subjective measurements.

Table 2 presents the results from a Chi-squared statistical study of the association between the level of adherence and controlled blood pressure. The level of adherence is divided into two groups, namely, patients with a high level of adherence and low adherence. Meanwhile, the therapy outcome group was divided into two, namely controlled and uncontrolled blood pressure.

Table 2. The correlation between the effect of adherence and treatment adherence based on the Medication Possession Ratio (MPR) and Medication Adherence Report Scale-5 (MARS-5)

Respondent Characteristics	Adherence Therapy of Hypertension Patients		(n= 85)	*p*-values	OR (95%CI)
	Controlled	Uncontrolled			
Adherence Therapy (MPR)					
Adherence	59 (69.4%)	6 (7.1%)	65 (76.5%)	0.000	18.262 (5.259-63.412)
Insufficient Adherence	7 (8.2%)	13 (15.3%)	20 (23.5%)		
Adherence Therapy (MARS-5)					
Adherence	59 (69.4%)	4 (4.7%)	63 (74.1%)	0.000	31.607 (8.170-122.277)
Insufficient Adherence	7 (8.2%)	15 (17.6%)	22 (25.9%)		

*Yates chi-square correction test; +Fisher Test; $p>0.05$ = not significantly correlated.
CI, confidence interval; OR, odds ratio.

The results of the analysis show that there is a significant relationship between adherence to therapy (MPR) and its therapeutic outcome targets (*p* value = 0.000), with patients who adhere to having an odds ratio (OR) of around 18.262 times higher to achieve success in therapy than those who do not comply. The same result also happened with therapy adherence (MARS-5), where the relationship was significant with therapy success (*p* value = 0.000), and adherent patients had approximately 31.607 times higher chances of achieving therapy success than those who were not adherent.

This study shows that high adherence with MARS-5 and MPR measurements will influence blood pressure control, reaching 69.4%. Successful therapy requires high patient adherence in taking medication. Low medication adherence might result in an inability to regulate the patient's blood pressure. The more compliant the patient is when taking medication, the better the blood pressure will be controlled (Alsofyani *et al*., 2022). However, there were also 7.1% (MPR) and 4.7% (MARS-5) of patients who had a high level of adherence but uncontrolled pressure which could be caused by several factors including lifestyle, food, and the stress level of each respondent which could influence pressure uncontrolled blood. Most hypertensive outpatients adhered to their medications well. Nevertheless, despite a generally high rate of adherence, observed inadequate blood pressure control indicates that changing one's lifestyle is crucial for managing hypertension (Pallangyo *et al*., 2022).

Apart from that, there were also low levels of adherence but controlled blood pressure of 8.2% in MPR and MARS-5 measurements. Before developing interventions to increase medication adherence, it is necessary to comprehend the multifaceted causes of poor medication adherence. The WHO categorizes the various variables that contribute to poor drug adherence into five groups: socioeconomic factors, therapy-related factors, patient-related factors, condition-related factors, and factors connected to the health system and health care team (HCT). A suitable intervention can then be individually designed to enhance each patient's medication-taking behavior once it is known whether the nonadherence is primary (starting pharmacotherapy) or secondary (implementing the prescribed regime) and what reasons have caused it (Lam and Fresco, 2015). Apart from that, the MPR measurement is only based on the amount of medication taken, but the reason cannot be known. Therefore, it is necessary to obtain more information for patients with low adherence.

As many as 15.3% (MPR) and 17.6% (MARS-5) of hypertensive patients were disobedient and did not control their blood pressure. The large number of patients who do not adhere to taking hypertension medication is caused by several factors. These factors include the fact that respondents felt better so they stopped treatment on their initiative and patients felt bored because they had to take medication every day without realizing that this decision could have fatal consequences, for example, it could cause other complications when blood pressure was not controlled. Apart from that, some patients also have excessive fear because the patient must take hypertension medication for life. This research is in line with (Ekarini *et al*., 2020) who explain several factors that influence patient non-adherence in taking medication, influenced by socio-demographics, level of knowledge, patient confidence in treatment, level of knowledge, boredom, and support from the surrounding family so that it will trigger blood pressure to become difficult to control. As a result, adherence to therapy is crucial to the success of treating hypertension. The patient's quality of life will increase and therapeutic success in the treatment of all chronic diseases will be achieved with adherence with appropriate drug use.

The relationship between therapy adherence (MPR and MARS-5) with ASCVD risk was measured in two categories, namely "Low" and "High" is shown in Table 3. According to the findings, there is a significant relationship between therapy adherence (MPR) and cardiovascular risk (*p* value = 0.020), with patients who are adhering having an OR that is almost 3.733 times higher to have low cardiovascular risk than those who are not. Correspondingly, stronger results were seen on therapy adherence (MARS-5), which showed a significant association with cardiovascular risk (*p* value=0.000), and adherent patients had approximately 9.000 times higher odds of having low cardiovascular risk than those who were disobedient.

Because hypertension is a condition that cannot be cured but must always be controlled to prevent consequences, adherence with therapy is a crucial component for hypertensive patients (Rosaria *et al*., 2017).

Table 3. The correlation between the effect of adherence and ASCVD Risk

Respondent Characteristics	ASCVD Risk		(n= 85)	*p*-values	OR
	Low Risk	High Risk			(95% CI)
Adherence Therapy (MPR)					
Adherence	40 (47.1%)	25 (29.4%)	65 (76.5%)	0.020	3.733
Insufficient Adherence	6 (7.1%)	14 (16.5%)	20 (23.5%)		(1.269-10.983)
Adherence Therapy (MARS-5)					
Adherence	42 (49.4%)	21 (24.7%)	63 (74.1%)	0.000	9.000
Insufficient Adherence	4 (4.7%)	18 (21.2%)	22 (25.9%)		(2.702-29.983)

*Yates chi-square correction test; +Fisher Test; $p>0.05$ = not significantly correlated.
CI, confidence interval; OR, odds ratio.

Because hypertension is a condition that cannot be cured but must always be controlled to prevent consequences, adherence with therapy is a crucial component for hypertensive patients (Rosaria *et al*., 2017).

At least more than 50% of hypertensive patients have cardiovascular risk. This occurs because persistent hardening of the blood vessels and lack of elasticity of the blood vessel walls (atherosclerosis) are causes of cardiovascular risk (PDHI, 2021). Table 3 shows a high level of adherence in hypertensive patients, reaching 47.1% (MPR) and 49.4% (MARS-5) who have a low risk of ASCVD. This low risk is associated with adherence to long-term use of antihypertensive drugs. The higher the level of adherence in using antihypertensives, the higher the potential for achieving blood pressure in the normal category, thereby minimizing high cardiovascular risk (Tumundo *et al*., 2021).

However, even at high adherence levels, 29.4% (MPR) and 24.7% (MARS-5) had a high risk of ASCVD. Several factors, such as gender, smoking status, age, and dyslipidemia can cause this increased risk. There is a relationship between age and smoking status on cardiovascular risk. Smoking and age are major risk factors for cardiovascular events. If these two factors occur simultaneously, it will accelerate the process of atherosclerosis thereby increasing cardiovascular risk (Djunaidi and Indrawan, 2014).

The low adherence rates of 7.1% (MPR) and 4.7% (MARS-5) resulting in a low risk of ASCVD could be due to several factors. Some factors that can have an influence are age and gender. Age is an unchangeable risk factor for cardiovascular disease. In the productive age, prevention of cardiovascular risk can be done (Yusvita and Nandra, 2018). This prevention approach is in line with the (WHO, 2020) statement, that increasing age is associated with the process of atherosclerosis where increasing age increases the cardiovascular risk process. Men and women are more at risk for cardiovascular disease when they are older than 55 and 65, respectively.

A total of 16.5% (MPR) and 21.2% (MARS-5) of patients had a low level of adherence with a high ASCVD risk result. Nearly 9% of all cardiovascular events in Europe are due to poor adherence, with adherence rates at only 57% (Piepoli *et al*., 2016). These data are supported by previous research that reported 45.2% of hypertensive patients were non-compliant, especially patients with uncontrolled blood pressure (Abegaz *et al*., 2017). In addition, several studies show that uncontrolled blood pressure will increase cardiovascular risk due to atherosclerotic formation which will make the heart work harder (Masenga and Kirabo, 2023; Yousuf *et al*., 2023).

This research has some limitations in the methods. The MPR method only assesses adherence to prescription refills without determining whether the patient actually consumes the medicine prescribed by the doctor. The MARS questionnaire method is subjective so using the questionnaire method has a tendency for patients to refrain from reporting non-adherence.

CONCLUSIONS

There is a relationship between adherence to taking medication with controlled blood pressure (BP <140/90 mmHg) and cardiovascular risk among hypertensive patients in Purworejo Regency. To have a higher impact on medication adherence, more initiatives to improve hypertension treatment adherence should be launched.

ACKNOWLEDGEMENTS

The authors would like to thank the Head and staff of Wirun Kutoarjo Primary Health Care, Purworejo, for their support during this study.

REFERENCES

Abegaz, T. M., Shehab, A., Gebreyohannes, E. A., Bhagavathula, A. S., Elnour, A.A. 2017. Nonadherence to antihypertensive drugs. *Medicine*, 96(4), e5641.

Adisa, R., Ilesanmi, O. A., Fakeye, T.O. 2020. Erratum: Treatment adherence and blood pressure outcome among hypertensive out-patients in two tertiary hospitals in Sokoto, Northwestern Nigeria, *BMC Cardiovascular Disorders*, 20(1), 1–10.

Akri, N. T., Nurmainah, N., Andrie, M. 2022. Analisis kepatuhan penggunaan obat antihipertensi pasien hipertensi rawat jalan usia geriatri terhadap tekanan darah. *Journal Syifa Sciences and Clinical Research*, 4(2), 437–446.

Alsofyani, M. A., Aloufi, A. O., Al-Qhtani, N. S., Bamansour, S. O., Almathkori, R.S. 2022. Factors related to treatment adherence among hypertensive patients: A cross-sectional study in primary healthcare centers in Taif city. *Journal of Family and Community Medicine*, 29(3), 181–188.

Anharudin, Tejamaya, M. 2022. Perbandingan risiko kardiovaskuler menggunakan metode Framingham, WHO Chart dan ASCVD pada pekerja PT. X tahun 2021. *Promotif: Jurnal Kesehatan Masyarakat*, 12(1), 77–84.

Asseggaf, S.N.Y.R.S., Ulfah, R. 2022. Analisa kepatuhan minum obat antihipertensi pada pasien peserta Posyandu Lansia Kartini Surya Khatulistiwa Pontianak. *Jurnal Pharmascience*, 9(1), 48.

Azmi, R. N., Lestari, D., Urahman, D., Tifana, S. 2021. Hubungan kepatuhan minum obat dengan outcome therapy antihipertensi pada geriatri di Panti Sosial Tresna Werdha Nirwana Puri Samarinda. *Jurnal Farmagazine*, 8(2), 8.

Chan, A. H. Y., Horne, R., Hankins, M., Chisari, C. 2020. The Medication Adherence Report Scale: A measurement tool for eliciting patients' reports of nonadherence. *British Journal of Clinical Pharmacology*, 86(7), 1281–1288.

Cheng, H., Gu, X., He, Z., Yang, Y. 2021. Dose-response relationship between working hours and hypertension: A 22-year follow-up study. *Medicine*, 100(16), e25629.

Clays, E., De Bacquer, D., Van Herck, K., De Backer, G., Kittel, F., Holtermann, A. 2012. Occupational and leisure time physical activity in contrasting relation to ambulatory blood pressure. *BMC Public Health*, 12(1).

Djunaidi, A., Indrawan, B. 2014. Hubungan usia dan merokok pada penderita penyakit jantung koroner di Poli Penyakit Dalam RS MH Palembang periode tahun 2012. *Syifa' MEDIKA: Jurnal Kedokteran dan Kesehatan*, 5(1), 16.

Dwivani, C., Herlina. 2018. Perbandingan lima metode estimasi risiko 10 tahun penyakit kardiovaskuler pada masyarakat Kabupaten Sleman-Yogyakarta. *JMPF*, 8(2), 59–69.

Ekarini, N. L. P., Wahyuni, J. D., Sulistyowati, D. 2020. Faktor-faktor yang berhubungan dengan hipertensi pada usia dewasa. *Jurnal Keperawatan*, 5(1), 61–73.

Erman, I., Damanik, H. D., Sya'diyah. 2021. DI PUSKESMAS KAMPUS PALEMBANG Politeknik Kesehatan Kemenkes Palembang, Sumatera Selatan, Indonesia. *Jurnal Keperawatan Merdeka*, 1(1), 54–61.

Gama, I. K., Sarmadi, I. W., Harini, I. 2014. Faktor penyebab ketidakpatuhan kontrol penderita hipertensi. *Jurnal Gema Keperawatan*, 65–71.

Hage, F. G., Mansur, S. J., Xing, D., Oparil, S. 2013. Hypertension in women. *Kidney International Supplements*, 3(4), 352–356.

Kane, J., Kissling, W., Lambert, T., Parellada, E. 2008. Adherence rating scales. *Centres of Excellence for Relapse Prevention*, 1–10.

Kemenkes RI. 2018. *Laporan Riskesdas 2018 Kementrian Kesehatan Republik Indonesia*. *Laporan Nasional Riskesdas 2018*.

Kozma, C., Dickson, M., Phillips, S., Meletiche, D. 2013. Medication possession ratio: Implications of using fixed and variable observation periods in assessing adherence with disease-modifying drugs in patients with multiple sclerosis. *Patient Preference and Adherence*, 7, 509-516.

Lam, W.Y., Fresco, P. 2015. Medication adherence measures: An overview. *BioMed Research International*, 2015, 1-12.

Liberty, I. A., Pariyana, P., Roflin, E., Waris, L. 2018. Determinan kepatuhan berobat pasien hipertensi pada fasilitas kesehatan tingkat I. *Jurnal Penelitian dan Pengembangan Pelayanan Kesehatan*, 1(1), 58–65.

Livana, P. H., Basthomi, Y. 2020. Triggering factors

related to hypertension in the city of Kendal, Indonesia. *Arterial Hypertension (Poland)*, 24(4), 181–191.

Manninda, R., Anggriani, Y., Sari, A.K. 2021. Analisis dampak program pengelolaan penyakit kronis (Prolanis) dalam meningkatkan outcome klinis pasien diabetes melitus tipe 2 di Puskesmas Jakarta, Indonesia. *Jurnal Ilmu Kefarmasian Indonesia*, 19(2), 237-244.

Masenga, S.K., Kirabo, A. 2023. Hypertensive heart disease: Risk factors, complications, and mechanisms. *Frontiers in Cardiovascular Medicine*, 10(June), 1–16.

Maulidina, F. 2019. Faktor-faktor yang berhubungan dengan kejadian hipertensi di wilayah kerja Puskesmas Jati Luhur Bekasi tahun 2018. *ARKESMAS (Arsip Kesehatan Masyarakat)*, 4(1), 149–155.

Mebrahtu, G., Moleki, M. M., Achila, O. O., Seyoum, Y., Adnoy, E. T., Ovberedjo, M. 2021. Antihypertensive medication adherence and associated factors: A cross-sectional analysis of patients attending a national referral hospital in Asmara, Eritrea. *Patient Preference and Adherence*, 15, 2619–2632.

Mortensen, M. B., Nordestgaard, B. G., Afzal, S., Falk, E. 2017. ACC/AHA guidelines superior to ESC/EAS guidelines for primary prevention with statins in non-diabetic Europeans: The Copenhagen General Population Study. *European Heart Journal*, 38(8), 586–594.

Pallangyo, P., Komba, M., Mkojera, Z. S., Kisenge, P. R., Bhalia, S., Mayala, H., Kifai, E., Richard, M. K., Khanbhai, K., Wibonela, S., Millinga, J., Yeyeye, R., Njau, N. F., Odemary, T. K., Janabi, M. 2022. Medication adherence and blood pressure control among hypertensive outpatients attending a tertiary cardiovascular hospital in Tanzania: A cross-sectional study. *Integrated Blood Pressure Control*, 15(August), 97–112.

PDHI. 2021. *Perhimpunan Dokter Hipertensi Indonesia*. *I-Hefcard.Com*, 118.

PERKI. 2022. *Panduan Prevensi Penyakit Kardiovaskular Arterosklerosis, Perhimpunan Dokter Spesialis Kardiovaskular Indonesia 2022*.

Piepoli, M. F., Hoes, A. W., Agewall, S., Albus, C., Brotons, C., Catapano, A. L., Cooney, M. T., Corrà, U., Cosyns, B., Deaton, C., Graham, I., Hall, M. S., Hobbs, F. D. R., Løchen, M. L., Löllgen, H., Marques-Vidal, P., Perk, J., Prescott, E., Redon, J., Richter, D. J., Sattar, N., Smulders, Y., Tiberi, M., Van Der Worp, H. B., Van Dis, I., Verschuren, W. M. M., Binno, S., De Backer, G., Roffi, M., Aboyans, V., Bachl, N., Carerj, S., Cho, L., Cox, J., De Sutter, J., Egidi, G., Fisher, M., Fitzsimons, D., Franco, O. H., Guenoun, M., Jennings, C., Jug, B., Kirchhof, P., Kotseva, K., Lip, G. Y. H., Mach, F., Mancia, G., Bermudo, F. M., Mezzani, A., Niessner, A., Ponikowski, P., Rauch, B., Stauder, A., Turc, G., Wiklund, O., Windecker, S., Zamorano, J. L., Achenbach, S. 2016. 2016 European guidelines on cardiovascular disease prevention in clinical practice. *European Heart Journal*, 37(29), 2315–2381.

Pratidina, D.B., Suryanegara, F.D. A., Nugraheni, D.A. 2021. Cost consequences analysis antihipertensi pasien rawat jalan: Studi di RS Swasta Daerah Istimewa Yogyakarta. *Jurnal Ilmiah Farmasi (Scientific Journal of Pharmacy)*, 17(2), 115–126.

Rahmadani, M. A., Sari, A. 2018. Kepatuhan terhadap pengobatan pada pasien hipertensi dengan komplikasi diabetes melitus di Puskesmas Yogyakarta. *Media Farmasi: Jurnal Ilmu Farmasi*, 15(2), 105.

RISKESDAS. 2018. *Laporan Hasil Riset Kesehatan Dasar (Riskesdas) Provinsi Jawa Tengah tahun 2018*. *Lembaga Penerbit Badan Penelitian dan Pengembangan Kesehatan*, 140–151.

Rosaria, K., Pratiwi, I., Perwitasari, M. 2017. Analisis faktor-faktor yang mempengaruhi kepatuhan pasien hipertensi dalam penggunaan obat di RSUD Kardinah. *Jurnal PoliTeknik Harapan Bersama Tegal*, 2, 204–205.

Runtuwene, W. N., Wiyono, W. I., Yudistira, A. 2019. Identifikasi tingkat kepatuhan pasien geriatri yang menderita hipertensi disertai penyakit penyerta di RSU Pancaran Kasih Manado periode September-Oktober 2018. *Pharmacon*, 8(1), 142.

Shaleha, R. R., Sumiwi, S. A., Levita, J. 2019. Pengaruh konseling terhadap kepatuhan minum obat dan tekanan darah pasien hipertensi terapi kombinasi di Poliklinik Tasikmalaya. *Jurnal Sains dan Teknologi Farmasi Indonesia*, 8(2), 39–47.

Srikartika, V. M., Cahya, A. D., Suci, R., Hardiati, W. 2016. Analisis faktor yang memengaruhi kepatuhan penggunaan obat pasien diabetes melitus tipe 2. *Jurnal Manajemen dan Pelayanan Farmasi*, 6(3), 205–212.

Taiso, S.N., Sudayasa, I.P., Paddo, J. 2021. Analisis hubungan sosiodemografis dengan kejadian hipertensi di wilayah kerja

Puskesmas Lasalepa, Kabupaten Muna. *Nursing Care and Health Technology Journal (NCHAT)*, 1(2), 102–109.

Tumundo, D.G., Wiyono, W.I., Jayanti, M. 2021. Adherence level of antihypertensive drug use in hypertension patients at Kema Health Center, North Minahasa Regency. *Pharmacon*, 10(4), 1121–1128.

Wahyuni, Eksanoto, D. 2013. Hubungan tingkat pendidikan dan jenis kelamin dengan kejadian hipertensi di Kelurahan Jagalan di wilayah kerja Puskesmas Pucangsawit Surakarta. *Jurnal Ilmu Keperawatan Indonesia*, 1(1), 112–121.

WHO. 2020. *Improving Hypertension Control in 3 Million People: Country Experiences of Programme Development and Implementation, Hearts*.

WHO. 2010. *World Health Statistics*.

Wibowo, M.I.N.A., Fitri, F.M., Yasin, N. M., Kristina, S. A., Prabandari, Y.S. 2021. Kepatuhan minum obat pada pasien diabetes melitus tipe 2 di beberapa Puskesmas Kabupaten Banyumas. *Jurnal Kefarmasian Indonesia*, 11(2), 98–108.

Yousuf, F.S., Khan, M.A.A., Bibi, R., Arif, A., Arshad, A., Almas, A. 2023. Medication adherence in patients with uncontrolled hypertension & hypertensive crisis presenting to a hospital setting in Karachi, Pakistan. *Cureus*, 15(1), 1–7.

Yusvita, F., Nandra, N. S. 2018. Gambaran tingkat risiko penyakit jantung dan pembuluh darah pada pekerja di PT X. *Forum Ilmiah Indonesia*, 15, 267–275.