



Adherence Assessment on Hypertension Therapy Using The Pill Count Method in Lubuk Kilangan Health Center, Indonesia

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ABSTRACT: Adherence is a major problem in hypertension treatment. Patients' adherence can be evaluated through pill count by counting the remaining amount of the patient's medication at the beginning and the end, using a pillbox as a tool to improve patient medication adherence. The purpose of this study was to describe the differences in adherence between patients who used the pillbox and without the pillbox. The research method used is Pretest-Posttest Control Group Design. The sample of this study is Prolanis (Chronic Disease Management Program) patients in 2021 at the Lubuk Kilangan Health Center in Padang City. They meet the inclusion and exclusion criteria that have been set. Sampling was carried out by total sample and obtained 70 subjects divided into the treatment group and the control group. The research technique used a Home Medication Review (HMR). The results of the study using the Mann-Whitney Test statistical test on adherence ($p = 0.007$) showed a value ($p < 0.05$). It can be concluded that there are differences in adherence before and after the intervention. This result indicates that adherence is higher in patients who use the pillbox than those without the pillbox.

Keywords: adherence; pillbox; home medication review; hypertension.

ABSTRAK: Kepatuhan merupakan masalah utama dalam pengobatan hipertensi. Kepatuhan pasien dapat dievaluasi melalui pill count dengan menghitung jumlah sisa obat pasien di awal dan di akhir, menggunakan *pillbox* sebagai alat untuk meningkatkan kepatuhan pengobatan pasien. Tujuan dari penelitian ini adalah untuk mendeskripsikan perbedaan kepatuhan antara pasien yang menggunakan *pillbox* dan yang tidak menggunakan *pillbox*. Metode penelitian yang digunakan adalah *Pretest-Posttest Control Group Design*. Sampel penelitian ini adalah pasien Prolanis (Program Penanggulangan Penyakit Kronis) tahun 2021 di Puskesmas Lubuk Kilangan Kota Padang. Mereka memenuhi kriteria inklusi dan eksklusi yang telah ditetapkan. Pengambilan sampel dilakukan dengan total sampel, dan diperoleh 70 subjek yang terbagi dalam kelompok perlakuan dan kelompok kontrol. Teknik penelitian menggunakan *Home Medication Review* (HMR). Hasil penelitian dengan uji statistik Mann-Whitney Test terhadap kepatuhan ($p = 0,007$) menunjukkan nilai ($p < 0,05$). Dapat disimpulkan bahwa terdapat perbedaan kepatuhan sebelum dan sesudah intervensi. Selain itu kepatuhan akan lebih tinggi pada pasien yang menggunakan *pillbox* dibandingkan yang tidak menggunakan *pillbox*.

Kata kunci: kepatuhan, pillbox, home medication review, hipertensi.

Introduction

World Health Organization (WHO) stated that in 2015, around 1.13 billion people worldwide suffered from hypertension, meaning that 1 in 3 people worldwide is diagnosed with hypertension. However, only 36.8% were taking medication, and as many as 9.4 million people died of hypertension. In addition, 45% of deaths were due to heart disease, and 51% were due to stroke caused by hypertension [1]. Furthermore, referring to the WHO, in 2019, the prevalence of hypertension globally was 22% of the world population, whereas Southeast Asia is in the 3rd highest position, with 25% of the total population [2].

According to a statement by the Ministry of Health

in 2018, hypertension is referred to as a "silent killer" so that usually, the person does not know he has hypertension and is only known after complications occur. The number of hypertension in Indonesia is on a reasonably large scale, as indicated by the prevalence of hypertension in the world which is increasing yearly. Hypertension is the number 3 cause of death after stroke and tuberculosis, reaching 6.7% of Indonesia's dead population of all ages [1].

Data Search by Basic Health Research (Riskesdas) in 2018 showed that hypertension in Indonesia was 34.1% compared to 27.8% in Riskesdas in 2013. The West Sumatra region's prevalence was 25.16% [3]. Generally,

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hypertension is associated with adult disease, but now it has begun to be associated with young age, namely the age of 15. According to the Padang City Health Service Report 2020, it was stated that of the 36,038 population aged 15 years or older who had blood pressure measurements taken, 21,878 people were served with a diagnosis of hypertension 60.7% [4].

Data from the World Health Organization (WHO) stated that 5070% of patients do not comply with prescribed antihypertensive drugs [5]. Based on the history and reasons for not taking medication based on a doctor's diagnosis in the hypertension population, 54.4% regularly took medicine, 32.3% did not take medicine regularly, and 13.3% did not take medication at all [3]. The report shows that the correct diagnosis, selection, and administration of the right drug by health workers is not enough to guarantee therapy success if it is not followed by patient compliance in taking the medication.

Measurement of compliance in this study used the pill count method by counting the remaining drugs objectively according to the number of drugs available [6]. The technical implementation used is a review of treatment at the patient's home called Home Medicines Review (HMR) to increase the use of appropriate drugs and reduce drug side effects in patients [7]. Furthermore, standardization of data collection is carried out during repeated visits [8]. Therefore, researchers are interested in analyzing the adherence to therapy of hypertensive patients with the pill count method in the Lubuk Kilangan Public Health Center, Padang City work area.

Method

Research Design

This research was conducted for three months in January-March 2022 in Lubuk Kilangan Health Center. Padang city. In this research design, the researcher used experimental research with the Pretest-Posttest Control Group Design [9]. This method was chosen because it only directly measured blood pressure at the last visit. In contrast, at the initial visit, only the results of measurements from patient medical records from the Lubuk Kilangan Health Center, Padang City, in 2021. Hypertensive patients who have filled out informed consent will receive hypertension medication as written on the prescription for 30 days. Patients in the control group will receive drugs in plastic packaging and patients in the intervention group will receive drugs in pillboxes. On the 30th day, the researcher will conduct a home visit and calculate the remaining drug in the patient. Hypertensive patients who have filled out

informed consent will receive hypertension medication as written on the prescription for 30 days. Patients in the control group will receive drugs in plastic packaging, and patients in the intervention group will receive drugs in pillboxes. On the 30th day, the researcher will conduct a home visit and calculate the remaining drug in the patient.

Population and Sampling

The sample in this study was adult patients with hypertension at the Lubuk Kilangan Health Center. From all medical record data from the Health Center, a sample was determined using a non-probability sampling method (purposive) following the characteristics that the researcher deliberately chose (inclusion and exclusion criteria) based on certain objectives and considerations. The minimum number of samples is determined with the equation used to determine the number of samples from a known population of less than 10000. The precision level specified in the sample's determination is 10% [10].

$$n = \frac{N}{N \cdot d^2 + 1}$$

Where, n = sample size, N = population < 10000, and d = margin of error/ corrected sampling.

Then, a random sample was determined using Microsoft Excel ($f_x = \text{RANDBETWEEN}$) so that the data for the control and treatment groups were objectively divided.

The inclusion criteria set in this study are: 1) adult patients with hypertension with or without other comorbidities who participated in Chronic Disease Management Program (Prolanis) for at least three months of treatment at the Lubuk Kilangan Health Center, Padang City in 2021; and 2) patients who are willing to participate in this study as evidenced by Informed Concentration. In addition, patients who died or moved to health facilities during the study were excluded from the study sample.

Data Analysis

Before the data analysis process, the distribution normality test was conducted to check whether the data obtained from each variable were normally distributed. This study's calculation of the normality test uses the Kolmogorov-Smirnov data normality test. A parametric test (paired T-test) can be used if the data is normally distributed. However, if the information is not homogeneous (not normally distributed), then the non-parametric test (Wilcoxon test) can be used [11].

In calculating using the pill count method, the

formula can be used equation by Grymonpre [12] :

$$\%Adherence = \frac{A - B}{CXD} \times 100$$

- A: The number of drugs given at the beginning
- B: Amount of final remaining drug
- C: Number of drugs taken per day
- D: The interval between the pre and post-date of the interview

Ethical Approval

Ethical approval was acquired from The Research Ethics Committee of Medical Faculty, Andalas University No 687/UN.16.2/KEP-FK/2022

Results and Discussion

Based on research carried out experimentally at the Lubuk Kilangan Health Center, 70 research subjects were obtained based on the inclusion and exclusion criteria set. The research subjects or samples were divided into two groups, namely the control and treatment groups. The division of groups was done randomly using Ms. Excel's "RANDBETWEEN " with 35 people each. The control group is the group that did not use the pill box, while the treatment group is the group that used the pill box.

The data on the sociodemographic characteristics of

hypertensive patients have been grouped based on gender, age, education level, and occupation, as shown in [Table 1](#).

The results of this study state that there is no significant difference between the control and treatment groups, with the majority of respondents in both groups [13]. Another study that showed the same results showed no significant difference in hypertension cases against gender. They stated that in almost all countries, the incidence of hypertension was higher in women than in men [14,15]. Gender factors affect the occurrence of hypertension, where more men suffer from hypertension than women, with a ratio of 2.29 for an increase in systolic blood pressure. In addition, men have a lifestyle that tends to increase blood pressure compared to women [16].

The more complex hormonal level of women compared to men is also one of the things that underlies the higher frequency of hypertension in women than men. The hormone estrogen can increase High-Density Lipoprotein (HDL) levels in women who have not experienced menopause. If HDL levels are high, it can prevent atherosclerosis, which acts as immunity for women who have not been menopausal [17–19]. In addition, the high number of female hypertension patients can also be influenced by the culture of society where women are more aware of the disease they are suffering from than men, so women are more likely to go to health services than men [20–22].

Table 1. Patient characteristics of the included study

Sociodemographic Characteristics	(Pillbox)		(Non-Pillbox)		p-value
	N=35	Percentage (%)	N=35	Percentage (%)	
Gender					
Male	7	20.00	9	25.71	0.569 ^a
Female	28	80.00	26	74.29	
Age (year)					
19-59	11	31.43	20	57.14	0.030 ^a
≥60	24	68.57	15	42.86	
Education level					
Low	22	62.86	16	45.71	0.277 ^b
Middle	11	31.43	14	40.00	
High	2	5.71	5	14.29	
Occupation					
Working	2	5.71	6	17.14	0.151 ^b
Not-working	33	94.29	28	80.00	

^a=Chi-Square test, ^b=Fisher's Exact Test, significant p<0.05

Table 2. Prescribing patterns in pill box and non-pill box in hypertension therapy

Antihypertensive drug	(Pillbox)		(Non-Pillbox)		p-value
	N=35	Percentage (%)	N=35	Percentage (%)	
Prescribing pattern					
Single	30	85.71	33	94.29	0.428
Combination	5	14.29	2	5.71	

Fisher's Exact Test, significant $p < 0.05$

If it is related to gender, more women suffer from hypertension at the age of 45 and over, and in general, women have experienced menopause symptoms at this age. Therefore, the sex of women over 45 years of age have a higher prevalence of hypertension than men of the same age. Along with increasing age, there will be degeneration or endurance, and the function of human organs begins to decline, so the risk of developing hypertension is higher [23]. Therefore, with increasing age, the risk of developing hypertension becomes greater. This condition is due to increasing age causes structural changes in large blood vessels so that the lumen and walls of blood vessels are inelastic and cause systolic blood pressure to increase [24].

The same opportunity to obtain education in all hypertensive patients causes no significant relationship between education level on knowledge and compliance of hypertensive patients. This result contrasted with the

results of research conducted by Alefan et al. (2019), which states that there is a significant difference in one's knowledge where patients who score high (95%) on knowledge are more obedient than those who score low (5%). It is also associated with a good patient lifestyle [16]. A person's level of education can affect how a person can receive and process the information obtained. This information will have an impact on the health status of the community [25–27]. A low level of education is related to the level of awareness of how a person behaves healthily. The low level of education of a person with a low level of knowledge and awareness can hinder the development of a person's attitude toward the information received so that the condition of hypertension is not well controlled [26]. However, a high level of education does not guarantee that the experience gained is also heightened due to socio-cultural influence according to their knowledge. In

Table 3. Distribution of antihypertensive regimen in pill box and non-pill box

Antihypertensive drug	(Pillbox)		(Non-Pillbox)	
	N=35	Percentage (%)	N=35	Percentage (%)
Gender				
Amlodipine 5 mg	27	77.14	23	65.71
Amlodipine 10 mg	2	5.71	9	25.71
Captopril 25 mg	1	2.86	0	0.00
Combination				
Amlodipine 5 mg + Candesartan 8 mg	1	2.86	0	0.00
Amlodipine 5 mg + Captopril 12.5 mg	0	0.00	1	2.86
Amlodipine 5 mg + Bisoprolol 2.5 mg	0	0.00	1	2.86
Amlodipine 10 mg +	0	0.00	1	2.86
Hydrochlorothiazide 25 mg	1	2.86	0	0.00
Amlodipine 10 mg + Candesartan 8 mg	1	2.86	0	0.00
Amlodipine 10 mg + Captopril 12.5 mg	1	2.86	0	0.00
Amlodipine 10 mg + Bisoprolol 2.5 mg	1	2.86	0	0.00
Captopril 12.5 mg + Hydrochlorothiazide 25 mg	1	2.86	0	0.00

addition, the average person also tends to be bored with taking drugs continuously [27].

Occupation is also an indicator that is one of the factors in determining a person's compliance, especially in the treatment of hypertension [23]. In this case, the occupation was classified into two groups: the working group and the non-working group consisting of homemakers and retirees.

Table 2 describes the prescribing patterns in hypertension therapy. The antihypertensive therapy can be initiated with a single drug therapy or a combination [28,29]. Combination therapy may be given if monotherapy does not respond. According to the Antihypertensive and Lipid-lowering Treatment (ALLHAT), to Prevent Heart Attack Trial only 26% of patients with blood pressure were controlled by using combination drugs. A second drug from a different class can be added if a single medicine at the usual dose cannot achieve the targeted blood pressure [28]. The longer the disease duration, the more frequent the medication, and the more complex the drug regimen, the worse the level of adherence to taking a person's medication [14,30].

In this study, most patients received a single antihypertensive therapy, as seen in Table 3. Nevertheless, according to Zappe et al. (2009), antihypertensive drugs are still effective when used as monotherapy, i.e., CCB (Calcium Channel Blocker) antihypertensive drugs. Therefore, for combined drug use, a thiazide diuretic with an ARB or CCB is generally recommended for patients requiring more than one antihypertensive drug [31].

In combination therapy, one person took Amlodipine with Hydrochlorothiazide (HCT). In the study by Zappe et al. (2009), as many as 67.8% of patients whose blood pressure was controlled by using amlodipine with HCT. However, there is a higher risk of peripheral edema when combined compared to amlodipine alone [31].

Nevertheless, those patients achieved the blood pressure target of 91% on captopril and 100% on amlodipine. In addition, he also stated that amlodipine has the best effectiveness compared to Captopril and HCT. Furthermore, the onset of action of amlodipine is slow, so it does not cause acute hypotension [32].

When given in combination, amlodipine and bisoprolol can reduce systolic blood pressure by 13.91 mmHg and diastolic by 3.48 mmHg. Therefore, the combination of these drugs is considered more effective when viewed from the effectiveness of treatment. However, when choosing amlodipine and bisoprolol treatment as first-line therapy, it must also be adjusted to the patient's other health conditions [33].

In this study, the measurement of the adherence level of hypertensive patients using the pill count method by calculating the patient's remaining medication expressed as a percentage of adherence, as seen in Table 4. For example, if the portion is 80%, it is categorized as "adherent"; if <80%, it is classified as non-adherent. The level of adherence in the pillbox group and non-pillbox group was observed before and after the intervention. The pill count calculation for both the control and treatment groups was carried out 30 days after the patient started taking hypertension medication from the health center. The difference between the two groups was that the treatment group was given a pill box as a container to put the patient's medicine. This process was conducted to observe the difference in the adherence level between patients who use the pill box and those who do not use the pill box.

From the study results, the treatment group (using the pill box) and the control group (not using the pill box) showed an increase in adherence results before and after the intervention was given. Both groups had improvement, but significant progress was seen in the treatment group

Table 4. Pill box and non-pill box hypertension patient adherence profile

Adherence profile	Adherence (≥80%)		Non-adherence (<80%)	
	N=35	Percentage (%)	N=35	Percentage (%)
Pill Box				
Initial	30	85.71	5	14.29
End	35	100.00	0	0.00
Non-Pill Box				
Initial	25	71.43	10	28.57
End	29	82.86	6	17.14

Table 5. Changes in the pill box and non-pill box hypertension patient adherence scores

Adherence score	X	ΔX	SE	p-value	
Pill Box					
Initial	89.38114	7.36	1.37	0.007	
End	96.746				
Non-Pill Box					
Initial	81.80914	0.48	2.91		
End	82.28571				

Mann Whitney Test, significant $p < 0.05$

compared to the control group. In the treatment group, there is a difference in adherence before and after the intervention in patients classified as adherence, which is 14.29%. Meanwhile, the control group only showed a difference of 11.43% in the number of visits.

Table 5 above shows the difference in the average and standard error of the adherence scores in the treatment group (using the pill box) and the control group (not using the pill box) before and after the intervention.

Based on the study results attached to the table above, it can be seen that in the difference in the average value of the treatment group given the pill box, there is an increase in the difference in the percentage of adherence of hypertension patients by 7.36. At the same time, the control group experienced an increase in the adherence rate with a value of 0.48. This value indicates an increase in adherence in both groups, but there is a significant increase in the treatment group.

There is an effect of pill boxes on the level of patient adherence to taking medication because using these tools increases patient adherence and helps patients take drugs that require long-term treatment, one of which is hypertension [34]. Pill boxes are also quite effective in overcoming adherence to regular medicines (drugs taken daily). In addition to the pillbox, it can improve adherence and the effect of therapy. It can also reduce the patient's therapy expenditure and improve their quality of life [35,36].

Strengths and Limitations

This study has several advantages because it uses data sourced from patient registration numbers, which are then matched with real conditions in the field. In addition, researchers go directly to the patient's home so that dishonesty in reporting drug use can be avoided. However, this research is limited to one sub-district, so it cannot represent other areas in the final conclusion.

Conclusion

Adherence to taking medication affects the success of treatment therapy. Meanwhile, some patients still do not comply with taking hypertension medication, which can be caused by several factors, including respondents who feel that their body condition is improving, so they think they can stop treatment on their initiative. In addition, some patients also have an excessive fear of taking hypertension drugs in the long term or for life. Optimal therapeutic results will not be achieved without the awareness of the patient himself. Therefore, it is essential to convince patients that hypertension drugs are safe to take continuously.

Authors' Contributions

NF is the principal investigator in this study. NF design ideas and techniques in research. FTA, KH, and YOS collect and rewrite medical record data on worksheets. LR did the grammar check. Furthermore, NF also performs data analysis and writes the manuscript.

Conflicting Interest

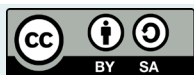
The author(s) declare no conflict of interest regarding this manuscript.

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References

- [1]. Widgery D. Health Statistics. Kurniawan R, Yudianto, Hardhana B, Siswanti T, editors. Vol. 1, Science as Culture. Jakarta: Departemen Kesehatan Republik Indonesia; 1988. 146–147 p. <https://doi.org/10.1080/09505438809526230>
- [2]. Departemen Kesehatan Republik Indonesia. Hipertensi Si Pembunuh Senyap. In: Kementerian Kesehatan RI. Jakarta: Departemen Kesehatan Republik Indonesia; 2019. p. 1–5.
- [3]. Laporan Nasional Riskesdas. Riset Kesehatan Dasar. Jakarta: Lembaga Penerbit Badan Penelitian dan Pengembangan Kesehatan (LBP); 2018.
- [4]. Dinas Kesehatan Kota Padang. Profil Kesehatan Tahun 2020. Padang: Dinas Kesehatan Kota Padang; 2021.
- [5]. World Health Organization. A global brief on Hypertension : Silent killer, global public health crisis (World Health Day 2013). WHO publication. Geneva: WHO Press; 2013. <https://doi.org/10.5005/ijopmr-24-1-2>
- [6]. Ulfa NM, Lubada EI, Darmawan R. Buku Ajar Farmasi Klinis dan Komunitas: Medication Picture dan Pill Count pada Kepatuhan Minum Obat Penderita Diabetes Mellitus dan Hipertensi. H. RN, editor. Gresik: Graniti; 2020.
- [7]. Emblen G, Miller E. Home medicines review. The how and why for GPs. Aust Fam Physician. 2004;33(1–2):49–51.
- [8]. Tan YM, Chong CP, Cheah YC. Impact of hospital pharmacist-led home medication review program for people with schizophrenia: A prospective study from Malaysia. J Appl Pharm Sci. 2019;9(7):034–41. <https://doi.org/10.7324/JAPS.2019.90705>
- [9]. Knapp TR. Why Is the One-Group Pretest-Posttest Design Still Used? Vol. 25, Clinical nursing research. United States; 2016. p. 467–72. <https://doi.org/10.1177/1054773816666280>
- [10]. Bolarinwa OA. Sample size estimation for health and social science researchers: The principles and considerations for different study designs. Niger Postgrad Med J. 2020;27(2):67–75. https://doi.org/10.4103/npmj.npmj_19_20
- [11]. Antony Stewart. Basic Statistics and Epidemiology. A practical guide. 4th ed. CRC Press; 2016.
- [12]. Grymonpre RE, Didur CD, Montgomery PR, Sitar DS. Pill count, self-report, and pharmacy claims data to measure medication adherence in the elderly. Ann Pharmacother. 1998;32(7–8):749–54. <https://doi.org/10.1345/aph.17423>
- [13]. Saputri ZG, Darmawan E, Farmasi F, Dahlan UA. Tingkat Kepatuhan Antihipertensi dan Pengontrolan Tekanan Darah Pasien Rawat Jalan RS PKU Muhammadiyah Bantul, Yogyakarta yang Mendapatkan Brief Counseling-5A dan SMS Motivasional. J Farm Sains dan Komunitas. 2016;13(2):67–72.
- [14]. Ernawati I, Lubada EI, Lusiyani R, Prasetya RA. Association of adherence measured by self-reported pill count with achieved blood pressure level in hypertension patients: a cross-sectional study. Clin Hypertens. 2022;28(1):12. <https://doi.org/10.1186/s40885-022-00195-5>
- [15]. Saepudin S. Kepatuhan Penggunaan Obat pada Pasien Hipertensi di Puskesmas. J Farm Indones. 2013;6(4):246–53.
- [16]. Alefan Q, Huwari D, Alshogran OY, Jarrah MI. Factors affecting hypertensive patients' compliance with healthy lifestyle. Patient Prefer Adherence. 2019;13:577–85.
- [17]. Wenger NK, Arnold A, Bairey Merz CN, Cooper-DeHoff RM, Ferdinand KC, Fleg JL, et al. Hypertension Across a Woman's Life Cycle. J Am Coll Cardiol. 2018;71(16):1797–813. <https://doi.org/10.1016/j.jacc.2018.02.033>
- [18]. Honigberg MC, Patel AP, Lahm T, Wood MJ, Ho JE, Kohli P, et al. Association of premature menopause with incident pulmonary hypertension: A cohort study. PLoS One. 2021;16(3):e0247398. <https://doi.org/10.1371/journal.pone.0247398>
- [19]. Staessen JA, Celis H, Fagard R. The epidemiology of the association between hypertension and menopause. J Hum Hypertens. 1998;12(9):587–92. <https://doi.org/10.1038/sj.jhh.1000670>
- [20]. Mills KT, Stefanescu A, He J. The global epidemiology of hypertension. Nat Rev Nephrol. 2020;16(4):223–37. <https://doi.org/10.1038/s41581-019-0244-2>
- [21]. Astutik E, Puspikawati SI, Dewi DMSK, Mandagi AM, Sebayang SK. Prevalence and Risk Factors of High Blood Pressure among Adults in Banyuwangi Coastal Communities, Indonesia. Ethiop J Health Sci. 2020;30(6):941–50. <https://doi.org/10.4314/ejhs.v30i6.12>
- [22]. Nuraini B. Risk Factors of Hypertension. J Major. 2015;4(5):10–9.
- [23]. Leigh JP, Du J. Hypertension and occupation among seniors. J Occup Environ Med. 2009;51(6):661–71. <https://doi.org/10.1097/JOM.0b013e31819f1d85>
- [24]. Mawaw PM, Yav T, Mukuku O, Lukanka O, Kazadi PM, Tambwe D, et al. prevalence of obesity, diabetes mellitus, hypertension and associated risk factors in a mining workforce, Democratic Republic of Congo. Pan Afr Med J. 2017;28:282. <https://doi.org/10.11604/pamj.2017.28.282.14361>
- [25]. Hussain MA, Mamun A Al, Reid C, Huxley RR. Prevalence, Awareness, Treatment and Control of Hypertension in Indonesian Adults Aged ≥40 Years: Findings from the Indonesia Family Life Survey (IFLS). PLoS One. 2016;11(8):e0160922. <https://doi.org/10.1371/journal.pone.0160922>
- [26]. Di Chiara T, Scaglione A, Corrao S, Argano C, Pinto A, Scaglione R. Education and hypertension: impact on global cardiovascular risk. Acta Cardiol. 2017;72(5):507–13. <https://doi.org/10.1080/00015385.2017.1297626>
- [27]. Pandit AU, Tang JW, Bailey SC, Davis TC, Bocchini M V, Persell SD, et al. Education, literacy, and health: Mediating effects on hypertension knowledge and control. Patient Educ Couns. 2009;75(3):381–5. <https://doi.org/10.1016/j.pec.2009.04.006>
- [28]. Tsioufis C, Thomopoulos C. Combination drug treatment in hypertension. Pharmacol Res. 2017;125(Pt B):266–71. <https://doi.org/10.1016/j.phrs.2017.09.011>
- [29]. Mancía G, Rea F, Corrao G, Grassi G. Two-Drug Combinations as First-Step Antihypertensive Treatment. Circ Res. 2019;124(7):1113–23. <https://doi.org/10.1161/CIRCRESAHA.118.313294>
- [30]. van Onzenoort HAW, Verberk WJ, Kessels AGH, Kroon AA, Neef C, van der Kuy P-HM, et al. Assessing medication adherence simultaneously by electronic monitoring and pill count in patients with mild-to-moderate hypertension. Am J Hypertens. 2010;23(2):149–54. <https://doi.org/10.1038/ajh.2009.207>
- [31]. Zappe D, Papst CC, Ferber P. Randomized study to compare valsartan ± HCTZ versus amlodipine ± HCTZ strategies to maximize blood pressure control. Vasc Health Risk Manag. 2009;5:883–92.
- [32]. Fadhillah SN, Permana D. The use of antihypertensive drugs in the treatment of essential hypertension at outpatient installations, Puskesmas Karang Rejo, Tarakan. Yars J Pharmacol. 2020;1(1):7–14.
- [33]. Gottwald-Hostalek U, Sun N, Barho C, Hildemann S. Management of Hypertension With a Fixed-Dose (Single-Pill) Combination of Bisoprolol and Amlodipine. Vol. 6, Clinical pharmacology in drug development. United States; 2017. p. 9–18. <https://doi.org/10.1002/cpdd.309>
- [34]. Choi EPH. A Pilot Study to Evaluate the Acceptability of Using a Smart Pillbox to Enhance Medication Adherence Among Primary Care Patients. Int J Environ Res Public Health. 2019;16(20). <https://doi.org/10.3390/ijerph16203964>
- [35]. Zeller A, Schroeder K, Peters TJ. Electronic pillboxes (MEMS) to assess the relationship between medication adherence and blood pressure control in primary care. Scand J Prim Health Care. 2007;25(4):202–7. <https://doi.org/10.1080/02813430701651954>
- [36]. Lam WY, Fresco P. Medication Adherence Measures: An Overview. Biomed Res Int. 2015;2015. <https://doi.org/10.1155/2015/217047>



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