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Original Article

Understanding Nonadherence to Antihypertensive Medications: Patterns, Predictors, Barriers, and Access Challenges in a Tertiary Care Setting in Libya

Sana Taher Ashur[1*], Rida Ben Fadel[2,3]

[1]*Department of Family and Community Medicine, Faculty of Medicine, University of Tripoli, Tripoli, Libya*
[2]*Department of Medicine, Faculty of Medicine, University of Tripoli, Tripoli, Libya*
[3]*Department of Cardiology, Tripoli University Hospital, Tripoli, Libya*
Correspondence email. drsana04@yahoo.com

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A B S T R A C T

Adherence to medications is crucial to achieving optimal control in chronic diseases, including hypertension. This study describes the characteristics of adherent and non-adherent patients on antihypertensive medication in a tertiary care setting in Libya. It further examines the subtypes of non-adherence, the perceived barriers associated with each subtype, the key predictors of non-adherence, and reports the medication access difficulties faced by all patients, regardless of their adherence status. The study utilized data from a larger cross-sectional study in one of the largest tertiary hospitals in Libya. The cohort for this analysis consisted of 320 patients with hypertension who had been on antihypertensive agents for more than 6 months. Data were obtained using structured interviews and medical records. The mean age of this cohort was 54.32 years (SD=10.39), and 60.3% were females. The prevalence of medication nonadherence was 34.9%. The most common subtype was unintentional non-adherence, accounting for 66.7% of non-adherents. Among the unintentional barriers, forgetfulness (55.0%) was the most frequently reported, whereas feeling well (21.6%) was the most prevalent intentional barrier. Overall, 68.5% of patients reported experiencing problems in accessing their medications, irrespective of their adherence status, with the majority reporting high cost as the main problem (93.1%). Predictors of medication nonadherence were irregular follow-up (P <0.001, OR=3.540, 95% CI: 1.982- 6.326), and no Home Monitoring of Blood Pressure (HMBP) (P = 0.006, OR=2.326, 95% CI: 1.275-4.244). In conclusion, medication non-adherence, predominantly the unintentional subtype, is considerable among hypertensive patients, with forgetfulness and feeling well-being the most prevalent barriers. Educational interventions about the importance of regular follow-up and HMBP, improving access to affordable medications, may improve medication adherence.

Introduction

Medication adherence is crucial in chronic diseases. Besides reduced therapeutic effects and disease progression [1], nonadherence has also been associated with increased hospital admissions and increased mortality [2]. Poor medication adherence also leads to more healthcare utilization [2] and, consequently, to significant economic consequences. Research has shown that nonadherence is associated with increased total costs [1-3], including direct costs related to healthcare, and indirect costs related to absenteeism and reduced work productivity [2]. Therefore, nonadherence to medications may impose a substantial cost burden on healthcare systems. Conversely, promoting medication adherence contributes to complications prevention, improves patients' quality of life [1, 4], and economic benefits [5].

In the context of hypertension, nonadherence to antihypertension therapy has been consistently linked to poor clinical outcomes like uncontrolled blood pressure and hypertension complications [6, 7]. Inadequate adherence is associated with increased all-cause hospital admission rates and all-cause mortality [6, 7]. It also inflates total health care costs [7]. Adequate adherence to antihypertensive medication has been shown to improve the quality of life of patients, particularly its physical and mental components [8].

Despite the importance of medication adherence, the global burden of inadequate adherence in chronic diseases remains high, especially in developing countries [5]. In the Middle Eastern countries, the estimated nonadherence rates in chronic diseases varied widely between 1.4 and 88% [9]. Focusing on hypertension, the reported global magnitude of nonadherence ranged from 27% to 40%, and research evidence consistently shows it is more prevalent in low and middle-income countries [6]. However, nonadherence in hypertension

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remains a significant challenge even in high-income countries. For instance, in the United Arab Emirates, up to 45.6% of hypertensive patients were found to be non-adherent to their medication [10].
Research has related the high rates of nonadherence in hypertension to various factors, including socio-demographic characteristics such as age [11, 12], educational level, and marital status [11], and clinical factors such as disease duration [12] and comorbidity [11]. Behavioral factors have also been linked to medication adherence in hypertension, including physical activity [13] and home monitoring of blood pressure [14]. Generally, insufficient self-care management was identified as a predictor of low medication adherence [15].
Despite the well-documented global and regional burden of medication nonadherence in chronic diseases, studies in Libya remain scarce and fragmented. A few studies were identified; however, they have primarily focused on diabetic patients [16-18], with no study dedicated to hypertension. A recent study examined medication adherence among the elderly, but did not address a disease-specific group [19]. Furthermore, while a previous study from the same research project examined medication adherence as an explanatory variable in relation to blood pressure control, it included patients regardless of their treatment duration, and without a specific focus on long-term medication adherence [20].
Therefore, the present study aims to provide a more refined analysis by focusing on a cohort of hypertensive patients who had been on medication for more than six months to better understand barriers to long-term adherence. Accordingly, this study describes the socio-demographic, clinical, and behavioral characteristics of adherent and non-adherent patients on antihypertensive medication in a large tertiary care setting in Libya. It further examines the subtypes of non-adherence, including its intentional, non-intentional, mixed, and unspecified subtypes, and the perceived barriers related to each subtype. The study also examines the key factors contributing to overall non-adherence. Additionally, it describes medication access problems faced by all hypertensive patients regardless of their adherence status.

Methods

This study is part of a larger research project on hypertensive patients undertaken from June through December 2023 at the cardiology outpatient department of Tripoli University Hospital, one of the largest hospitals in Libya. The main project is designed to focus on different outcomes relevant to hypertension, including blood pressure control [20]. For the parent study, the sample size was calculated to estimate the prevalence of uncontrolled hypertension, and the required sample size was 347. Patients were conveniently invited to take part in the study, and 335 responses were obtained.
For this cohort, where the analysis focused on medication adherence, only data of patients who had been placed on antihypertensive medications for more than six months were included. This was applied to ensure the assessment of established long-term medication adherence patterns, distinct from the initial period of medication titration and adjustment. Patients who reported not being prescribed antihypertensive medications yet, or who had shorter treatment durations, were excluded. After applying these criteria, the final sample size was 320 participants (Figure 1). Post-hoc sample size calculations were performed using the single proportion formula [21], with nonadherence rates of 82.4% [22], 65.8% [23], and 57.8% [24] from other Arab populations. The obtained sample sizes ranged from 223 to 377, which supports the sufficiency of the final sample considered for the analysis.

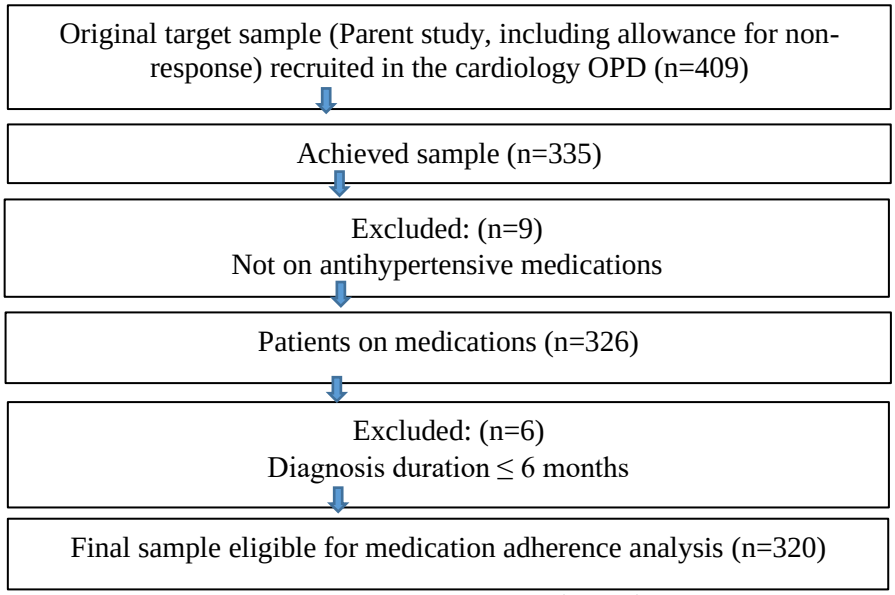

Figure 1. Participants Flow chart

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The primary outcome variable was medication adherence status (adherent versus non-adherent). Explanatory variables included socio-demographic characteristics (sex, age, education, occupation, and monthly income), clinical characteristics (e.g., disease duration, number of prescribed medications, antihypertensive regimen complexity [number of antihypertensive medications], concomitant use of lipid lowering therapy, over-the-counter medications [OTC] use, and comorbidity), and selected hypertension self-management behaviors (dietary pattern, physical activity, Home Blood Pressure Monitoring [HBPM], and follow-up regularity). Exploratory variables were problems in accessing medications among all participants and barriers to medication adherence among non-adherents.

Data were collected using an interviewer-based questionnaire and patients' medical records. Medication adherence was assessed by self-report through a single question," Do you regularly take your prescribed antihypertensive medications exactly as directed by your doctor?", with yes and no responses. Although prone to underestimation of non-adherence, the use of a single-item to measure medication adherence is recognized in the literature, mainly for its utility as a practical and efficient tool. Several studies supported the use of single-item medication adherence measures. For instance, grounded by The Transtheoretical Model of behavioral change (TTM), research showed a strong correlation between the one-item medication adherence tool and patients' readiness to medication [25]. Furthermore, a single-item measure reported to predict hospitalization and death in heart failure patients among non-adherents [26], and its concurrent validity was demonstrated by showing a strong correlation with blood pressure levels in hypertensive patients [27].

Data analysis was run using the SPSS software, version 26. Frequency and percentages were used to present the categorical variable, while mean and standard deviation or median and interquartile range were used as appropriate to summarize continuous data. Chi-square test, independent t-test, and Mann-Whitney test were used to examine the bivariate association between the explanatory variables and medication adherence. Adjusted multivariate analysis, using logistic regression, was conducted to examine the predictors of non-adherence to medication. A p-value of ≤0.05 is considered statistically significant.

Results

Table 1 summarizes the sociodemographic, clinical, and behavioral characteristics of the participants. The mean age was 54.32 years (SD=10.39), and females comprised 60.3% of the participants. Approximately two-fifths of the participants had low education (39.1%), and more than half of them were not employed (53.0%), with a median monthly income of 900 Libyan dinars (LD) (IQR: 600-1500). Of all participants, 43.1% were on a single antihypertensive regimen, and 60.6% were not on concomitant lipid-lowering therapy. Of all participants, 132 (41.3%) reported OTC medication use concurrently with their prescribed antihypertensive medications. The most commonly reported medications were paracetamol (19.4%), non-steroidal anti-inflammatory drugs (NSAIDs) (17.2%), and Aspirin (5.9%). Other miscellaneous medications were reported by a small number of participants (0.3-2.2%). Half of the participants reported being on a low salt diet (50.2%), but only 20.0% were physically active. More than half of the participants were not monitoring their blood pressure at home (52.6%), and 38.4% were not visiting their doctor for 6 months or longer.

Table 1 also presents the prevalence of nonadherence to medication and the bivariate association between various patients' characteristics and medication adherence status. Of the 320 eligible participants, only 318 reported their medication adherence status, and the prevalence of nonadherence was 34.9%. The subtypes of non-adherence are presented below in relation to the reported barriers (Tables 3 and 4).

Of all socio-demographic characteristics, only occupation showed a significant association with medication adherence (p=0.044), with non-adherence being less common among professional and skilled workers (20.6%) compared with manual workers (36.1%) and non-employed patients (37.7%). All hypertension self-management behaviors showed statistically significant associations with medication adherence. A significant association was observed between dietary pattern and medication adherence (p<0.001), with the rate of non-adherents being higher among patients who consume a conventional Libyan diet (47.2%) than that among those who follow a low salt diet (22.2%). Nonadherence was significantly higher among physically inactive patients (38.9%) than among those who reported being physically active (21.2%) (p=0.001). Also, nonadherence was significantly higher among patients who do not monitor their blood pressure at home (47.8%) compared with those who monitor their blood pressure (22.0%) (p<0.001). Additionally, a significant association was found between follow-up regularity and medication adherence (<0.001), and the rate of nonadherence was significantly higher among patients who reported irregular follow-up (55.5%) compared with those who were on regular follow-up (23.3%) (p<0.001).

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Table 1. Sociodemographic, clinical, and behavioral characteristics of patients on antihypertensive medications (n=320) and comparison by their medication adherence status (n=318)

Characteristics	All (n=320)		Medication Adherence Status				P value
			Adherent (n=207)		Non-adherent (n=111)		
	F	(%)	F	(%)	F	(%)	
Medication adherence status (n=218)							
Adherent	207	(65.1)					
Non-adherent	111	(34.9)					
Socio-demographic							
Sex							
Females	193	(60.3)	121	(63.0)	71	(37.0)	0.338
Males	127	(39.7)	86	(68.3)	40	(31.7)	
Age (yrs), (mean ±SD)[a]	54.32	±10.39	54.33	±10.97	54.41	±9.32	0.948
Education (n=317)							
Low (Primary or no education)	124	(39.1)	72	(58.5)	51	(41.5)	0.053
Intermediate (Secondary school/ diploma)	135	(42.6)	88	(65.2)	47	(34.6)	
University degree or higher	58	(18.3)	44	(77.2)	13	(22.8)	
Occupation (n=315)							
Professional/skilled	64	(20.3)	50	(79.4)	13	(20.6)	0.044*
Manual / service	84	(26.7)	53	(63.9)	30	(36.1)	
Non-employed (Housewife, retired, unemployed)	167	(53.0)	104	(62.3)	63	(37.7)	
Monthly income (LD), median (IQR) [b]	900	(600-1500)	900	(600-1500)	810	(500-1200)	0.135
Clinical characteristic							
Disease Duration (yrs), median, (IQR) [b]	6	(3-10)	5	(2-9)	5.81	(3-10)	0.191
Total prescribed meds (mean ±SD)[a]	2.56	±1.22	2.58	±1.22	2.56	±1.23	0.883
Antihypertensive Regimen complexity [c]							
Single-drug Regimen	138	(43.1)	85	(62.5)	51	(37.5)	0.649
Two-drug Regimen	`119	(37.2)	81	(68.1)	38	(31.9)	
Multi-drug Regimen	63	(19.7)	41	(65.1)	22	(34.9)	
Concomitant Lipid-lowering therapy							
Yes	126	(39.4)	78	(61.9)	48	(38.1)	0.334
No	194	(60.6)	129	(67.2)	63	(32.8)	
OTC use							
Yes	132	(41.3)	84	(64.1)	47	(35.9)	0.761
No	188	(58.3)	123	(65.8)	64	(34.2)	
Comorbidity							
Yes	130	(40.6)	129	(68.6)	59	(31.4)	0.113
No	190	(59.4)	78	(60.0)	52	(40.0)	
Hypertension self-management behaviors							
Dietary pattern (n=319)							
Conventional Libyan diet	159	(49.8)	84	(52.8)	75	(47.2)	0.000**
Low-salt	160	(50.2)	123	(77.8)	35	(22.2)	
Physical activity (n=315)							
Active	63	(20.0)	50	(82.0)	11	(21.2)	0.001*
Inactive	252	(80.0)	154	(61.1)	98	(38.9)	
HBPM (n=302)							
Yes	143	(47.4)	110	(78.0)	31	(22.0)	0.000**
No	159	(52.6)	83	(52.2)	76	(47.8)	
Follow-up regularity (n=310)							
Regular (Monthly & 3-4 months)	191	(61.6)	145	(76.6)	44	(23.3)	0.000**
Irregular (≥ 6 months)	119	(38.4)	53	(44.5)	66	(55.5)	

** p<0.05, ** p<0.001, [a] Based on an Independent t-test, [b] Based on a Mann-Whitney test, [c] Antihypertensive Regimen complexity was defined as the number of antihypertensive agents prescribed.*

Overall, 68.5% of all participants reported experiencing problems in accessing their antihypertensive medications, irrespective of their adherence status, with the vast majority reporting high cost "medication is expensive," as the main problem (93.1%) (Table 2).

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Table 2. Access to medications among all participants (n=317)

Access problem	f	(%)
Experienced an access problem	217	(68.5)
Reason for the problem*		
Medication is too expensive	202	(93.1)
Not available at the pharmacy	21	(9.7)
No cash on hand	36	(16.6)
Reported no access problem	100	(31.5)

**Percentages for specific reasons are calculated out of the 217 participants who reported any access problem. Total exceeds 100% as participants could report more than one reason*

Among non-adherent participants, barriers to antihypertensive medication were classified into intentional and unintentional categories (Table 3). The most common unintentional barriers to adherence were forgetfulness (55.0%), followed by lack of cash money, which is an access barrier (30.6%), whereas the most prevalent intentional barrier was feeling well and deciding to stop taking medicine (21.6%). Based on the reported barriers, nonadherence was further categorized into four subtypes (Table 4). The most common subtype was unintentional non-adherence (66.7%).

Table 3. Barriers to medication adherence reported among non-adherents (n=111)

Barriers category and type	f	(%)
Unintentional		
Forgetfulness	61	(55.0)
Lack of cash (Access barrier)	34	(30.6)
Unavailability of the drug at the pharmacy (Access barrier)	8	(7.2)
Intentional		
Feeling well (deciding to stop)	24	(21.6)
Fear of side effects	2	(1.8)

Total exceeds 100% as participants could report more than one barrier.

Table 4. Subtypes of nonadherence among non-adherent participants (n=111)

Subtype of non-adherence	f	(%)
Unintentional nonadherence only	74	(66.7)
Intentional non-adherents only	13	(11.7)
Mixed nonadherence (both intentional and unintentional*	13	11.7
Barrier not specified	11	(9.9)

** Participants reported at least one intentional and at least one unintentional barrier*

All variables that showed a significant association (p ≤0.05) or a nearly significant association (p<0.25) with medication adherence status were considered in a multivariate logistic regression. However, one variable (monthly income) in the resultant model had a standard error < 0.001, indicating model instability; therefore, income was omitted, and the regression was re-run to produce a stable model (28). (Table 5) shows the final built model for the predictors of nonadherence to antihypertensive medications. This model showed a good fit of the included data as indicated by a non-significant Hosmer-Lemeshow test (p > 0.05). Referencing Nagelkerke R, this model explains 28.1% of the variance of nonadherence to medications, with an accuracy of 74.5%. Of all included variables, only two significant variables maintained a significant contribution to medication nonadherence variance, both of which were self-management behaviors. In order of the strength of their statistical association based on the Wald statistic, these were follow-up regularity and HMBP. Hypertensive patients who reported irregular follow-up (≥ 6 months) were three and a half times more likely to be not adherent to their antihypertensive medications compared with those who reported regular follow-up (P <0.001, OR=3.540, 95% CI: 1.982- 6.326), and patients who do not measure their blood pressure at home were twice as likely to be non-adherent compared with patients who monitor their blood pressure at home (P=0.006, OR=2.326, 95% CI: 1.275-4.244).

Table 5. Multivariable logistic regression model of predictors of nonadherence to antihypertensive medication

Variable	B	P	Adj. OR	(95% CI)
Education		0.512		
Low vs University degree and higher	0.257	0.621	1.293	(0.467-3.580)
Intermediate vs University degree and higher	0.483	0.292	1.621	(0.660-3.981)

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Occupation		0.231		
Non-employed vs Professional/skilled	0.781	0.089	2.185	(0.887-5.381)
Manual/service vs Professional/skilled	0.574	0.209	1.776	(0.725-4.350)
Disease duration	0.002	0.925	1.002	(0.954-1.053)
Comorbidity (No vs Yes)	-0.356	0.227	0.701	(0.393-1.248)
Diet (Conventional vs Low-salt diet)	0.441	0.152	1.554	(0.851-2.838)
Physical activity (Inactive vs Active)	0.802	0.067	2.229	(0.946-5.253)
HBPM (No vs Yes)	0.844	0.006*	2.326	(1.275-4.244)
Follow-up regularity (Irregular vs Regular)	1.264	0.000**	3.540	(1.982-6.326)
Constant	-3.240	0.000**	0.043	

*$p<0.05$, **$p<0.001$

Discussion

The study revealed a considerable burden of nonadherence to medications among hypertensive patients (34.9%). While the estimated rate falls within the globally reported range of nonadherence in hypertension (27% to 40%) [6], it is much higher than the rate found among hypertensive patients in Saudi Arabia (12.3%) [29], and lower than the rates reported in the United Arab Emirates (45.6%) [10], and Tunisia (83.2%) [15]. This inconsistency could be attributed to several factors, such as the differences in study populations, healthcare settings, and methods used to measure medication adherence.

Nonadherence was most commonly due to unintentional causes. The most frequently cited barrier leading to unintentional nonadherence was forgetfulness. Consistently, forgetting to take medications is commonly reported among hypertensive patients [30], and it has been identified as a predictor of medication adherence in several studies [10, 31]. Additionally, regardless of adherence status, a significant proportion of the participants reported experiencing medication access challenges, with cost being the most common problem. This finding is of particular concern, as research has shown that medication cost contributes to nonadherence [32]. Therefore, unaffordability of medication could further exacerbate unintentional non-adherence, especially in the context where patients have to purchase medications out-of-pocket. from private pharmacies.

Pure intentional nonadherence was not common (11.7%), with the most prevalent intentional barrier causing this type being feeling well and deciding to stop taking medicine. This reason was commonly reported in research; for instance, almost one-quarter of non-adherent hypertensive patients in a Pakistani study reported stopping taking medications for feeling no need to take them regularly [33]. This reflects the importance of considering the patient as an active partner in the clinical consultation and explaining the asymptomatic nature of hypertension and the necessity of continuing medications to them.

Patients with follow-up gaps longer than 6 months were less likely to be non-adherent to their medications. Irregular follow-up was also identified as a significant predictor of nonadherence in other studies [32, 34, 35]. This shows the importance of the follow-up visit as an opportunity to reinforce medication continuity. Additionally, patients who do not monitor their blood pressure at home had higher odds of being non-adherent to their medications, which is consistent with some other studies [36]. Home monitoring of blood pressure empowers patients as active partners in their disease management and thus enhances their adherence.

Although OTC use did not contribute to medication adherence status in this analysis, it is noteworthy to emphasize that a substantial proportion of OTC medication use was observed in this cohort. The most commonly reported types were paracetamol and NSAIDs. Given that NSAIDs can interfere with blood pressure control, especially with long-term use [37, 38], and some recent studies suggest a similar impact for the concomitant use of paracetamol with antihypertensive medications [39, 40], further research is warranted to explore OTC use in hypertension. This should include not only OTC types of medications, but also their use frequency and duration to distinguish between occasional and chronic use.

This single-center study provided valuable insights into medication adherence in hypertension through a refined analysis in one of Libya's largest tertiary centers. The focus of this study on long-term adherence, subtypes, and predictors adds to its rigor. However, several limitations should be considered in the interpretation of the findings. The single-center design limits the generalizability of the findings, particularly as the parent sample from which this study was derived was not randomly selected. Besides, the use of a self-reported, single-item measure of medication adherence, while practical and efficient for the current study, is subject to social disability and recall bias. This could lead to an underestimation of non-adherence. Further multicenter research using a validated multi-item adherence scale is recommended to confirm and extend these study findings. In addition, future investigations on OTC medication use in hypertension should examine the types, frequency, and duration of use, as well as the potential pharmacological interactions with antihypertensive therapy. Moreover, interventional studies are recommended to evaluate

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whether educational interventions on safe OTC use can mitigate these risks and support adherence. Nevertheless, the findings from this study can inform practice and policy. Interventions should address the identified barriers and modify the nonadherence predictors. Since forgetfulness was the most commonly reported adherence barrier, healthcare providers should support their patients through clearly communicating the use instructions of the medications, repetition, and encouraging note-taking during consultation. As a considerable proportion of patients reported that they intentionally decided to stop medications when they feel well, health education should emphasize the asymptomatic nature of hypertension, and the importance of continuing medications. Education of patients should also stress the importance of regular follow-up and blood pressure monitoring at home, as they are two strong predictors of medication adherence. Furthermore, as the cost was the most frequently reported access challenge, relevant health authorities should ensure the consistent availability and affordability of antihypertensive medication in public pharmacies, to reduce the need for patients to purchase them out-of-pocket.

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