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Barriers to up-titrated antihypertensive strategies in 12 sub-Saharan African countries: the Multination Evaluation of hypertension in Sub-Saharan Africa Study

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Background: Sub-Saharan Africa (SSA) faces the highest rate of hypertension worldwide. The high burden of elevated blood pressure (BP) in black people has been emphasized. Guidelines recommend two or more antihypertensive medications to achieve a BP control. We aimed to identify factors associated with prescription of up-titrated antihypertensive strategies in Africa.

Methods: We conducted a cross-sectional study on outpatient consultations for hypertension across 12 SSA countries. Collected data included socioeconomic status, antihypertensive drugs classes, BP measures, cardiovascular risk factors and complication of hypertension. We used ordinal logistic regression to assess factors associated with prescription of up-titrated strategies.

Results: The study involved 2123 treated patients with hypertension. Patients received monotherapy in 36.3 vs. 25.9%, two-drug in 42.2 vs. 45% and three and more drugs strategies in 21.5 vs. 29.1% in low (LIC) and middle (MIC) income countries, respectively. Patients with sedentary lifestyle [OR 1.4 (1.11–1.77)], complication of hypertension [OR 2.4 (1.89–3.03)], former hypertension [OR 3.12 (2.3–4.26)], good adherence [OR 1.98 (1.47–2.66)], from MIC [OR 1.38 (1.10–1.74)] and living in urban areas [OR 1.52 (1.16–1.99)] were more likely to be treated with up-titrated strategies. Stratified analysis shows that in LIC, up-titrated strategies were less frequent in rural than in urban patients (*P* for trend <0.01) whereas such difference was not observed in MIC.

Conclusion: In this African setting, in addition to expected factors, up-titrated drug strategies were associated with country-level income, patient location and finally, the interplay between both in LIC. These results highlight the importance of developing policies that seek to make multiple drug classes accessible particularly in rural and LIC.

Keywords: hypertension, cardiology, antihypertensive medications, developing countries

Abbreviations: ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; BP, blood pressure; CCB, calcium channel blockers; EIGHT study, Evaluation of hypertension in Sub-Saharan Africa Study; OR, odds ratio; RAS blockers, renin–angiotensin system blockers; SSA, sub-Saharan Africa; β blockers, beta-blockers

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INTRODUCTION

The burden of noncommunicable disease (NCD) is alarmingly increasing worldwide, especially in low-income and middle-income countries [1]. High blood pressure (BP) is a major risk factor for several common NCD like stroke, heart failure, and chronic kidney failure [2,3]. Sub-Saharan Africa (SSA) faces the highest rate of hypertension worldwide with an overall prevalence estimation of 46% [1,4,5]. 74.7 millions of people could suffer from hypertension and this figure is expected to reach 216.8 million by 2030 [6,7].

The high burden of elevated BP in black people has been related to genetic factors, epigenetic adaptation to climate, and increased salt intake [8–12]. The percentage of events attributable to hypertension was higher in blacks (36%) than in whites (21%) [13].

Hypertension control rests on the association of lifestyle modification and blood pressure-lowering medications [14]. Guidelines on appropriate antihypertensive strategies for management of hypertension based on multiple clinical trials conducted in high-income countries are available [13–15]. In black adults, the previous WHO guidelines in 2013 recommended a sequential treatment with up-titrated strategies starting with a calcium channel blocker (CCB) or a diuretic in monotherapy and combining both drugs only in case of inadequate BP control [5]. The American 2015 [16], European 2013 [17] and ISH 2014 [18] guidelines recommend, especially in black adults with hypertension, two or more antihypertensive medications to achieve a BP target of less than 130/80 mmHg. Despite the high burden of hypertension in Africa, there are few randomized clinical trials (RCT) evaluating the best treatment for hypertension in SSA [14,19,20] and studies on African-Americans or African-Caribbeans are not necessarily generalizable to SSA populations because of both contrasting environmental settings and genetic diversity [21]. Observational studies provide a description of practice and are an essential step in setting up RCTs. However, there is scarce information from SSA [22,23]. Published data are derived from worldwide studies, where SSA countries are poorly represented [24] or estimated [25].

This question was addressed in the EIGHT study (Evaluation of Hypertension in Sub-Saharan Africa). This cross-sectional study conducted in 12 SSA countries, aims to describe and analyze BP control through multiple dimensions: socioeconomic status [26], adherence [27], cultural factors [28] and antihypertensive drugs prescribed [29]. The EIGHT study underlined a high proportion of patients with hypertension at least 180/110 mmHg still treated with monotherapy. Thereby, analysis of up-titrated strategies (monotherapy, two-drug strategies, three and more drugs strategies) should be investigated.

Here, in this article, we aim to describe prescriptions of up-titrated strategies in African black adults in real clinical practice and identify factors associated with prescriptions of up-titrated strategies.

METHODS

Study design and setting

The EIGHT study was a cross-sectional study conducted using data collected during outpatient consultations for

hypertension in cardiology departments of 29 hospitals from 17 cities across 12 SSA countries [Benin, Cameroon, Congo (Brazzaville), Democratic Republic of the Congo, Gabon, Guinea, Côte d'Ivoire, Mauritania, Mozambique, Niger, Senegal, Togo] between January 2014 and November 2015.

A multidisciplinary collaborative team of epidemiologists, cardiologists and pharmacists from Africa and France conceived and designed The Evaluation of Hypertension among Patients in Africa (EIGHT) study.

The EIGHT team had extensive prior research experience and existing collaborations with a network of physician-scientists in Africa in the field of access to treatment, such as quality of cardiovascular drugs [30], which aided the planning and launching of the present study.

The study was approved by the Ile-de-France III ethics committee (number 2014-A00710-47) and was declared to the National Commission of Informatics (number 1762715). This study was exclusively supported by a public grant.

Participants

Patients at least 18 years of age with treated hypertension were enrolled at any visit during outpatient consultations in the cardiology departments of the participating hospitals. Each patient received an information leaflet about the study. In addition, the on-site physician presented and explained the study in the regional language to all patients meeting eligibility criteria. Patients who agreed to participate completed a standardized questionnaire while waiting for their appointment. Participating physicians at each center received a training note detailing the study and standardized instructions on how they should interact with the patients while completing the questionnaire.

Measurements

A dedicated questionnaire was conceived for this study [26]. A pilot investigation involving 90 patients who tested the questionnaire was conducted in Côte d'Ivoire.

Country level income

The country income level was obtained from the World Bank database (<http://data.worldbank.org/country>, accessed 12 January 2015) and categorized into low-income and middle-income countries.

Collected data

The first part of the questionnaire was completed by patients and collected data on patient sociodemographic factors (age, sex, and patient location), use of traditional medicine and adherence to treatment. A patient was defined as nonadherent if she/he reported forgetting to take medications the day before the outpatient consultation.

The second part was filled out by the physician during the consultation and collected data on socioeconomic status (patient wealth index), antihypertensive drugs classes and generic prescriptions, blood pressure values (measured in standardized conditions, see below), BMI, cardiovascular risk factors and complication of hypertension. The antihypertensive drug classes recorded were: calcium channel blockers, diuretics, renin-angiotensin system blockers

(including angiotensin-converting enzyme inhibitors and angiotensin receptor blockers), beta-blockers, centrally active drugs and direct vasodilators.

Patient wealth index were assessed by the treating physician and classified as low, middle and high:

1. 'Low' defined patients who have difficulties to afford medical consultations.
2. 'Middle' defined patients who can manage with paying medical consultations.
3. 'High' defined patients who have no difficulties to pay medical consultations.

Blood pressure measurement

Seated office BP was measured twice by the physician, at least 15 min apart; participants were instructed to avoid caffeine and smoking within 30 min prior to BP measurement.

Uncontrolled hypertension was defined by a SBP at least 140 mmHg and/or a DBP of at least 90 mmHg on either of the measured office BP values in the clinic [17].

Severity of hypertension was defined according to guidelines available at the time of the study, that is, 2013 ESH/ESC guidelines [17]: mild hypertension (SBP: 140–159 mmHg and/or DBP: 90–99 mmHg), moderate hypertension (SBP: 160–179 mmHg and/or DBP: 100–109 mmHg) and severe hypertension (SBP \geq 180 mmHg and/or DBP \geq 110 mmHg).

Antihypertensive drug strategies

Antihypertensive drug strategies were defined according to the number of prescribed drug classes and constitute three levels: monotherapy, two-drug strategies and three and more drugs strategies. Prescriptions of up-titrated antihypertensive drug strategies are defined by moving from a less intensive strategy to a more intensive therapeutic strategy. Prescriptions of up-titrated antihypertensive drug strategies also refers to the concept of optimizing treatment in relation to the severity of the patient's hypertension with the ultimate goal of achieving blood pressure control.

Study power

The study was designed with 90% power to detect a relative difference greater than 5% on BP control between monotherapy and combination therapy (with a significance level of 5%). A total of 2060 patients were required. In this article, we calculated a retrospectively study power of 90%.

Statistical analysis

Continuous and categorical variables were expressed as mean (standard deviation) and numbers (percentage) wherever appropriate. Student test and chi-square tests were used to compare continuous and categorical variables wherever appropriate.

Ordinal logistic regression analysis was used to study factors associated with up-titrated antihypertensive drug strategies considered as an ordinal variable (range 1, 2 and 3 corresponding to monotherapy, two-drug strategies and three and more drugs strategies); odds ratio (OR) and 95% confidence intervals were computed. First, univariate analysis was conducted on sociodemographic, clinical and

treatment factors and a *P* value less than 0.20 was selected to enter into multivariate analysis. A fixed effect for country was added to account for intercountry variability. Then, a multivariate analysis was conducted using a stepwise method with age, sex and patient wealth index forced into the models to adjust on sociodemographic factors. To avoid multicollinearity (e.g. country and country-level income), only country-level income was maintained in the multivariate model.

Furthermore, we quantified the association between up-titrated strategies and patient location (urban vs. rural) stratifying on country-level income to investigate if hypertension management was influenced by patient location separately in low-income and middle-income countries.

Sensitivity analysis

To strengthen results, we performed two sensitivity analysis: analysis of factors associated with up-titrated strategies was repeated after contrasting two-drugs, three drugs and more strategies vs. monotherapy using multinomial logistic regression, and analysis of factors associated with up-titrated strategies was repeated using ordinal logistic regression after considering patients with uncontrolled hypertension only.

Regression analyses were computed on complete cases only. A two-tailed *P* value of less than 0.05 was considered significant. All analyses were performed through scripts developed in the R software [version 3.5.1 (2018-07-02)].

RESULTS

Participants

The multination EIGHT study involved 2123 hypertension patients treated by drugs in 12 SSA countries. Overall, 994 patients (46.8%) were from six low-income countries (Benin, Democratic Republic of the Congo, Guinea, Mozambique, Niger, and Togo), and 1129 (53.2%) were from six middle-income countries [Cameroon, Congo (Brazzaville), Gabon, Côte d'Ivoire, Mauritania, and Senegal].

In both low-income and middle-income countries, most patients were living in urban areas (77.9 and 80%, respectively). Overall, 71.6% of hypertensive patients had at least one cardiovascular risk factor. Among cardiovascular risk factors (other than hypertension), sedentary lifestyle was the most reported one (38.9%).

Overall, 625 (38.3%), 543 (33.3%) and 462 (28.3%) patients had mild, moderate and severe hypertension, respectively. Most patients ($n = 1771$, 85%) were diagnosed with hypertension for more than 1 year prior to inclusion to the survey. Characteristics of patients by country-level income and by strategies are presented in Table 1. Patients were more often obese (15.3 vs. 25.5%) and with complication of hypertension (47.3 vs. 41.9%) in low vs. middle-income countries.

Treatments

Patients received monotherapy in 36.3 vs. 25.9%, two-drug strategies in 42.2 vs. 45% and three and more drug strategies in 21.5 vs. 29.1% in low-income and middle-income countries, respectively. Strategies differed according to country-level income ($P < 0.001$). Among patients treated by monotherapy, 73.7% were adherent to treatment in

TABLE 1. Characteristics of patients by level-income countries and by antihypertensive strategies

	Overall						Low income			Middle income		
	Antihypertensive strategies (N)						Two-drugs therapy			Monotherapy		
	Monotherapy	Two-drugs therapy	Three-drugs and +	Global	Monotherapy	Two-drugs therapy	Three-drugs and +	Global	Monotherapy	Two-drugs therapy	Three-drugs and +	Global
	361	419	214	994	292	508	329		508	329	1129	
Age (year), mean (SD)	58.38 (11.7)	57.45 (11.9)	58.92 (11.2)	57.7 (11.4)	58.21 (12.39)	59.51 (12.2)	58.93 (11.0)		59.51 (12.2)	58.93 (11.0)	59.0 (11.9)	
Male [N (%)]	852 (40.1)	151 (41.8)	94 (43.9)	438 (44.1)	97 (33.2)	192 (37.8)	125 (38.0)		192 (37.8)	125 (38.0)	414 (36.7)	
Patient wealth index [N (%)]												
Low	361 (17.4)	55 (15.7)	23 (11.0)	139 (14.3)	54 (18.9)	105 (21.2)	63 (19.6)		105 (21.2)	63 (19.6)	222 (20.1)	
Middle	1017 (49.0)	141 (40.3)	94 (44.8)	415 (42.7)	161 (56.5)	270 (54.4)	171 (53.1)		270 (54.4)	171 (53.1)	602 (54.6)	
High	697 (33.6)	154 (44.0)	93 (44.3)	418 (43.0)	70 (24.6)	121 (24.4)	88 (27.3)		121 (24.4)	88 (27.3)	279 (25.3)	
NA	48	11	4	22	7	12	7		12	7	26	
Patient location (urban vs. rural) [N (%)]	1646 (79.1)	253 (72.1)	167 (80.3)	756 (77.9)	232 (80.0)	393 (79.1)	265 (81.5)		393 (79.1)	265 (81.5)	890 (80.0)	
NA	41	10	6	24	2	11	4		11	4	17	
Cardiovascular risks factors [N (%)]												
At least one	1141 (71.6)	185 (65.6)	157 (77.3)	594 (72.9)	130 (67.4)	244 (68.0)	173 (76.2)		244 (68.0)	173 (76.2)	547 (70.2)	
Tobacco use	77 (4.8)	6 (2.1)	7 (3.4)	31 (3.8)	10 (5.2)	27 (7.5)	9 (4.0)		27 (7.5)	9 (4.0)	46 (5.9)	
Diabetes mellitus	280 (17.6)	55 (19.5)	39 (19.2)	173 (21.2)	19 (9.8)	40 (11.1)	48 (21.1)		40 (11.1)	48 (21.1)	107 (13.7)	
Hypercholesterolemia	324 (20.3)	54 (19.1)	81 (39.9)	239 (29.3)	21 (10.9)	38 (10.6)	26 (11.5)		38 (10.6)	26 (11.5)	85 (10.9)	
Hypertriglyceridemia	88 (5.5)	20 (7.1)	12 (5.9)	62 (7.6)	6 (3.1)	13 (3.6)	7 (3.1)		13 (3.6)	7 (3.1)	26 (3.3)	
Obesity	324 (20.3)	29 (10.3)	41 (20.2)	125 (15.3)	50 (25.9)	89 (24.8)	60 (26.4)		89 (24.8)	60 (26.4)	199 (25.5)	
Sedentary lifestyle	620 (38.9)	99 (35.1)	85 (41.9)	310 (38.0)	70 (36.3)	128 (35.7)	112 (49.3)		128 (35.7)	112 (49.3)	310 (39.8)	
None	453 (28.4)	97 (34.4)	46 (22.7)	221 (27.1)	63 (32.6)	115 (32.0)	54 (23.8)		115 (32.0)	54 (23.8)	232 (29.8)	
NA	529	79	11	179	99	149	102		149	102	350	
BMI [mean (SD)]	27.91 (5.83)	26.99 (5.28)	28.46 (5.94)	27.55 (5.53)	28.35 (5.78)	28.17 (6.49)	28.21 (5.62)		28.17 (6.49)	28.21 (5.62)	28.23 (6.06)	
Hypertension severity [N (%)]												
Mild	625 (38.3)	119 (40.8)	54 (34.0)	283 (38.2)	93 (41.0)	160 (40.8)	89 (33.0)		160 (40.8)	89 (33.0)	342 (38.5)	
Moderate	543 (33.3)	100 (34.2)	52 (32.7)	258 (34.8)	80 (35.2)	120 (30.6)	85 (31.5)		120 (30.6)	85 (31.5)	285 (32.1)	
Severe	462 (28.3)	73 (25.0)	53 (33.3)	200 (27.0)	54 (23.8)	112 (28.6)	96 (35.6)		112 (28.6)	96 (35.6)	262 (29.5)	
NA	493	69	55	253	65	116	59		116	59	240	
Year since hypertension diagnosis (> 1 year) [N (%)]	1771 (85.0)	272 (77.1)	191 (92.3)	825 (84.6)	215 (74.9)	440 (88.4)	291 (89.8)		440 (88.4)	291 (89.8)	946 (85.3)	
NA	39	8	7	19	5	10	5		10	5	20	
Complication of hypertension (a least one vs. none) [N (%)]	909 (44.4)	131 (37.2)	142 (67.0)	459 (47.3)	87 (30.9)	210 (43.4)	153 (49.5)		210 (43.4)	153 (49.5)	450 (41.9)	
NA	77	9	2	23	10	24	20		24	20	54	
Use of traditional medicine [N (%)]	488 (23.7)	75 (21.4)	35 (17.2)	226 (23.6)	75 (26.6)	115 (23.0)	72 (22.7)		115 (23.0)	72 (22.7)	262 (23.8)	
NA	66	11	11	36	10	8	12		8	12	30	
Prescription of generic drug [N (%)]	796 (50.7)	160 (59.7)	147 (72.1)	502 (64.4)	65 (33.9)	103 (28.1)	126 (54.1)		103 (28.1)	126 (54.1)	294 (37.2)	
NA	552	93	10	214	100	142	96		142	96	338	
Adherent to treatment [N (%)]	1802 (84.9)	266 (73.7)	193 (90.2)	808 (81.3)	251 (86.0)	446 (87.8)	297 (90.3)		446 (87.8)	297 (90.3)	994 (88.0)	

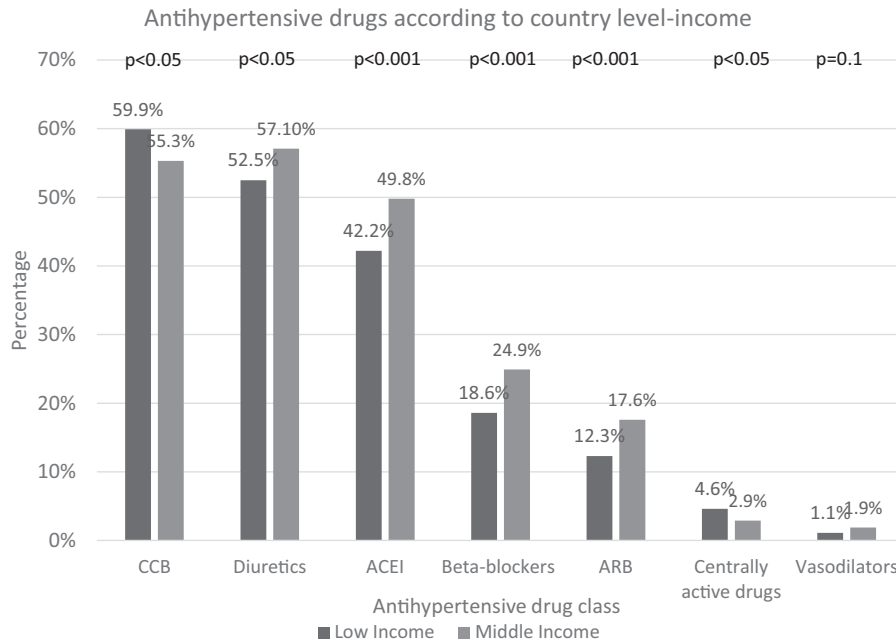


FIGURE 1 Antihypertensive drugs according to country-level income. ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; CCB, calcium channel blockers.

low-income countries compared with 86% in middle-income countries.

Antihypertensive drug classes according to country-level income are presented in Fig. 1. Overall, RAS blockers [angiotensin-converting enzyme inhibitors (ACEI) + angiotensin receptor blockers (ARB)] were the classes most widely prescribed (61.3%, $n = 1302$). CCB were more prescribed in low than in middle-income countries (59.9 vs. 55.3%, $P < 0.05$). On the contrary, diuretics, ACEI, β blockers and ARB were more often prescribed in middle than in low-income countries ($P < 0.05$).

Strategies by drug classes according to country-level income are depicted in Fig. 2. In low-income countries, diuretics were more frequently prescribed in monotherapy (15.7 vs. 6.2%) and CCB in two-drug therapy (40.7 vs. 34.3%), than in middle-income countries. In middle-income countries, β blockers (60.1 vs. 49.7%) and ACEI (42.6 vs. 34.2%) were most widely prescribed as a part of three drugs strategies than in low-income countries. In both country level income, vasodilators and centrally active drugs were prescribed as a part of three and more drugs strategies.

Factors associated with up-titrated antihypertensive strategies

Factors associated with up-titrated antihypertensive strategies in univariate analysis are detailed in Supplemental Table 1, <http://links.lww.com/HJH/B956>.

The factors associated with up-titrated antihypertensive strategies in multivariate analysis are reported in Fig. 3. Patients with sedentary lifestyle [OR 1.4 (1.11–1.77), $P < 0.05$], with complications of hypertension [OR 2.4 (1.89–3.03), $P < 0.01$], diagnosed with hypertension for more than 1 year [OR 3.12 (2.3–4.26), $P < 0.01$], who are adherent [OR 1.98 (1.47–2.66), $P < 0.01$], from middle-income

countries [OR 1.38 (1.10–1.74), $P < 0.01$] and living in urban areas [OR 1.52 (1.16–1.99), $P < 0.01$] were more likely to be treated with up-titrated strategies.

We further stratified the analysis by country-level income and investigated the association between patient location and up-titrated strategies. In middle-income countries, proportions of antihypertensive strategies did not differ according to patient location (urban or rural) (P for trend = 0.6) (Fig. 4). In low-income countries, proportions of antihypertensive strategies differed according to patient location (P for trend < 0.01). In this setting, rural patients received more frequently monotherapy (45.8 vs. 33.5%) but less often two-drug strategies (35 vs. 44%) and three and more drug strategies (19 vs. 22%) than urban patients, respectively.

Sensitivity analysis

Similar results were observed in multinomial logistic regression contrasting multi-therapies strategies (two-drugs, three and more drugs) VS monotherapy.

When analysis was restricted to uncontrolled patients (76.7%, $n = 1630$), the same determinants of up-titrated strategies as in main analysis were retrieved (sedentary lifestyle, complication of hypertension, year since diagnosis, adherence to medication, country-level income and patient location).

DISCUSSION

The EIGHT study represents the first sub-Saharan African multinational report on the determinants of antihypertensive strategies. We investigated factors associated with prescriptions of up-titrated antihypertensive strategies in 12 African countries. As expected, adherent patients, those with sedentary lifestyle, complication of hypertension and

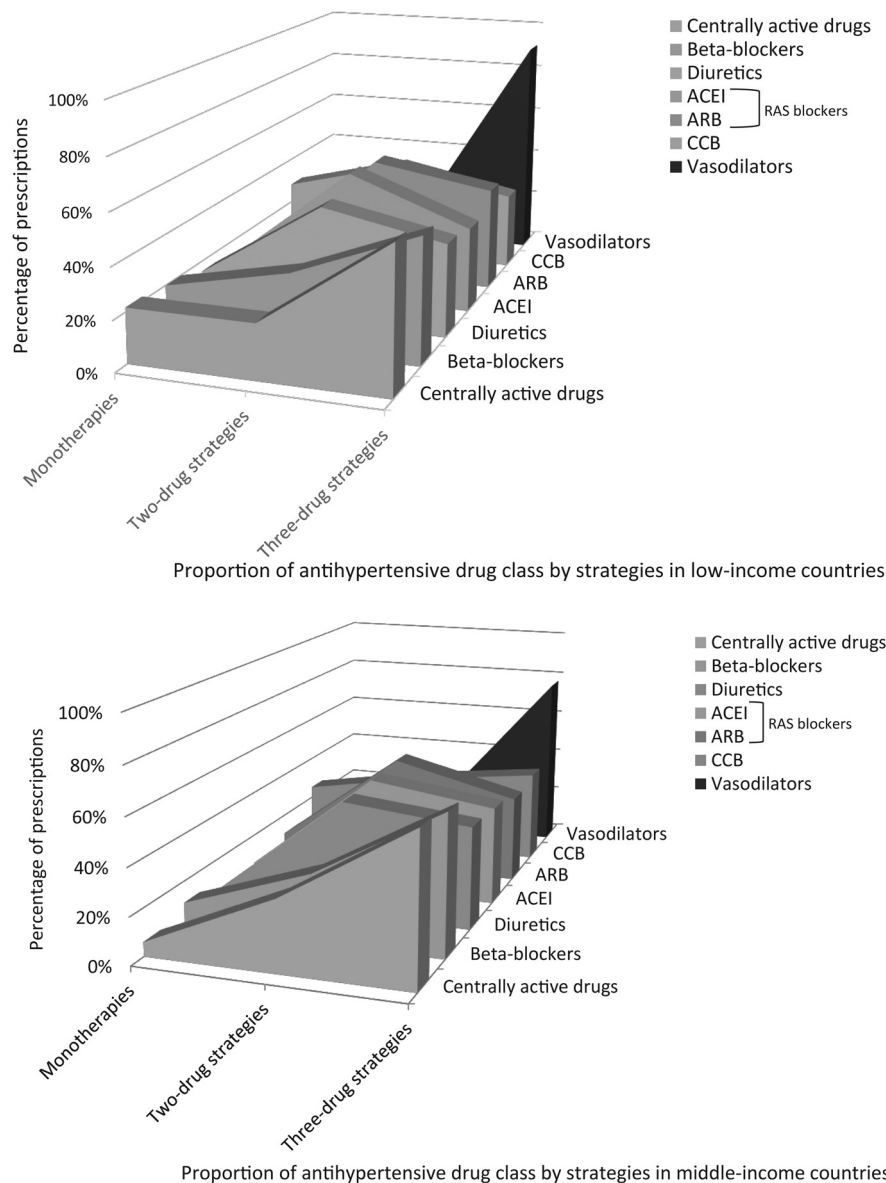


FIGURE 2 Strategies and drug classes according to country-level income. ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; CCB, calcium channel blockers.

hypertension diagnosed for more than 1 year were treated with more intensive antihypertensive strategies. Novel findings include the influence of country income level and patient location on the likelihood of up-titrated strategies. Our results highlighted barriers to up-titrated strategies: patients from low-income countries (as compared with middle-income countries) and those from rural location (compared with urban location) were less susceptible to be treated with up-titrated strategies. Moreover, in low-income countries, rural patients remained more treated with monotherapy than urban patients, whereas this was not observed in middle-income countries.

Several international and African guidelines exist to manage hypertension [4,14,31–33]. These guidelines recommended various treatments and prioritize different patients [34]. It could be difficult for physicians to navigate

between the different guidelines and resources available in their country. In SSA countries, five dimensions of access to medicine should be considered including availability, affordability, accessibility, acceptability and quality of medicines [35]. Acceptability describes how medicines are used in real-world settings, including appropriate prescriptions by physicians and behavior of patients (adherence and cultural factors) [35]. Our study underlined the interplay between acceptability and accessibility of treatments. Our study highlighted that acceptability by physicians varied also according to country-level income and patient location. In the African context, physicians had to adjust their therapeutic strategies to sociodemographic characteristics, such as patient wealth index, country-level income and patient location. Physicians also adapt their prescriptions to the accessibility of the patient's treatment, which may be

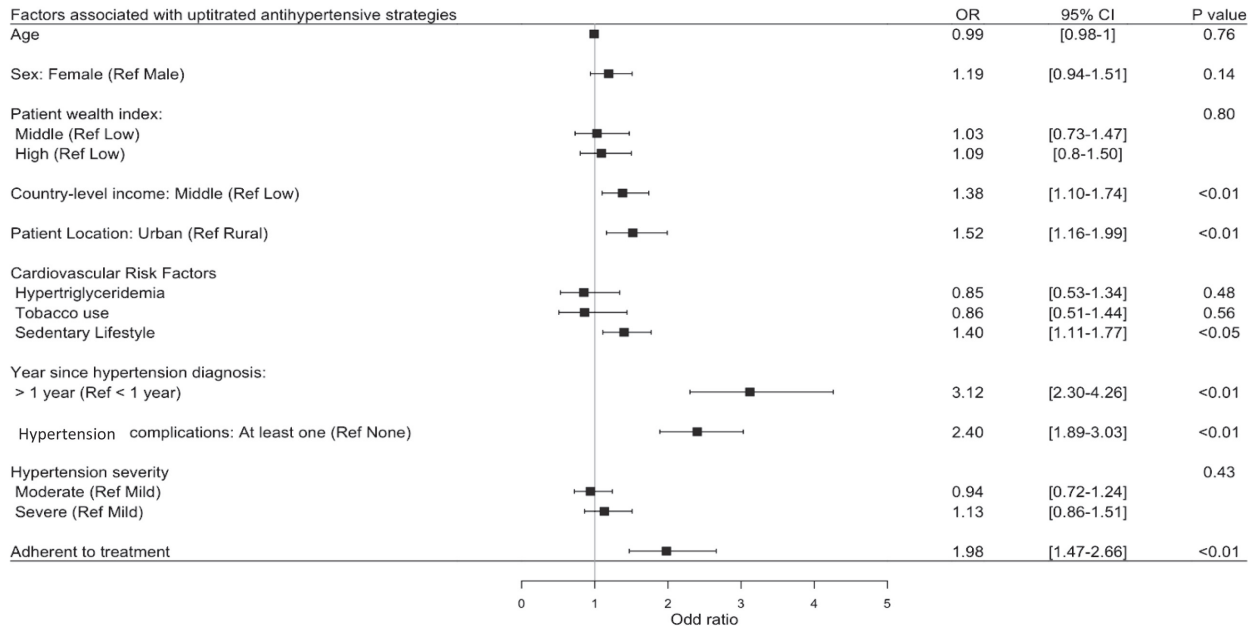


FIGURE 3 Odds ratio of factors associated with up-titrated antihypertensive strategies among treated patients in multivariate analysis. Squares represent odds ratio (OR) and lines, 95% confidence interval (CI). ORs derived from ordinal logistic regression with the stepwise method.

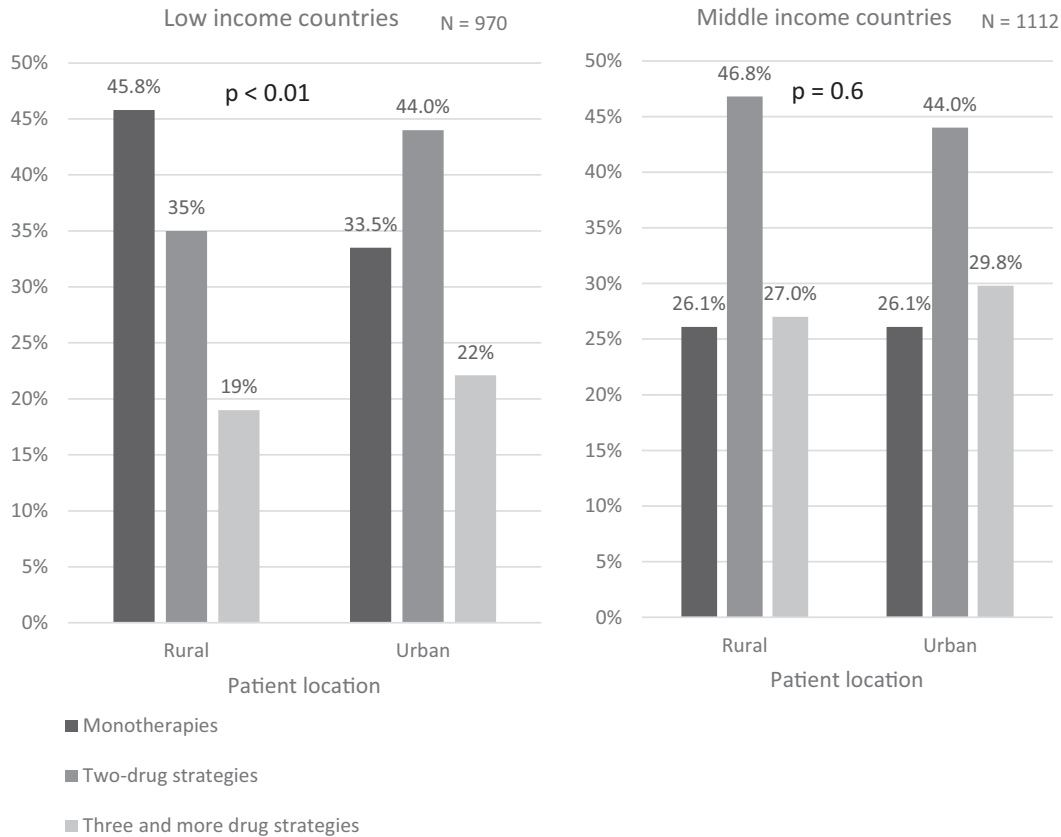


FIGURE 4 Antihypertensive strategies according to country-level income and patient location.

more difficult in rural areas. This highlights that individual location combined with a poor health system can contribute to an unhealthy synergy, representing a ‘double hit’. The recent ISH 2020 guideline explicitly account for the

local health economics context, and therefore, making distinctions in up-titrated strategies whenever drugs are not available [36]. In a recent study, a novel model of care tried to improve blood pressure control in SSA by

standardizing the management of hypertension and using smartphones and regular check-ins to ensure optimal patient follow-up [37]. Even if this model could be a part of the solution it is worth considering whether such a model could be generalized to low-income and middle-income countries without including cultural and environmental elements [38].

The WHO tried to improve access to medicines by establishing a list of essential medicines that should be available in each country [39]. In the same way, polypill seems to be effective to increase adherence to medicines, and thus, blood pressure control but even if a patient has a prescription for polypill, they may be unable to purchase or access this treatment [14,20]. Furthermore, the 2021 WHO guidelines also emphasize the importance of combination therapy in low-income countries [33]. Generic drugs could have a lower cost and could constitute a solution to improve the medicines in Africa. In our study, we observed a difference between proportion of prescription of generic (VS brand product) between low-income and middle-income countries. Physicians prescribed more generics in low-income than in middle-income countries. In the same way, patient do not have systematically the choice in drugstore between lowest priced generic or original brand product because of the lack of treatment availability and accessibility [40].

Studies, such as the present one are useful to obtain hard data from the field and suggest that different strategies may be needed in low-income vs. middle-income countries in order to push towards achieving adequate hypertension management in the population. In addition, improvement in public health care delivery, adequate quality control measures, increase access to diagnostic tools and low-cost generic medications of quality are all essential elements to attain an effective public health strategy to tackle the growing menace of hypertension. Improvement of hypertension cascade of care at a population level will require strategies beyond improvement of each five dimensions of access to blood pressure-lowering medicines. Additional barriers imposed by providers, health systems and patient characteristics are important factors for achieving blood pressure control [41].

Limitations and strengths

We acknowledge the following limitations. Caution is needed in extrapolating the information in the current study to other African populations as the sampling framework in each country was not nationally representative. The data in the EIGHT study were derived from urban hospitals and likely represents the best-case scenario for BP treatment. Although a random selection of centers would be ideal from a methodological perspective, such an approach is not practical, given the lack of cardiovascular care in this part of the world. We can fear we have overestimated blood pressure figures, and therefore, uncontrolled hypertension because of the white-coat effect during one visit. We tried to consider this effect by measuring seated office BP twice by physicians. We chose this measure as it was appropriate for the African setting. Defining uncontrolled hypertension vs. controlled hypertension based on office blood pressure readings during one visit was open to criticism but we

cannot be sure that patients will ever come back in outpatient consultation. Furthermore, given the observational nature of the study, the reported associations should not be interpreted as being causal. This study could not take into account the role of indication bias in interpreting cross-sectional associations between drug regimens and hypertension severity. We cannot exclude residual confounding by time on treatment. We may have even underestimated the nonadherence to treatment as we used self-reported questionnaire [42]. However, self-reported medication adherence is the simplest way to assess nonadherence during outpatient visits, especially in LMICS where more accurate methods of nonadherence detection including urine drug detection by LCMSMS, are very complex to deploy. Also, evidence pointed out that self-reported adherence is predictive of clinical outcomes and especially in hypertensive patients [43,44].

Strengths of the study includes its multisite design including 29 hospitals from 17 cities in 12 countries, and its relatively large sample size with over 2000 patients. Actual data on management of cardiovascular disease are uncommon in Africa and are usually derived from small, single-center studies. The EIGHT study embraced 12 sub-Saharan African countries, which are usually not considered in international studies. Furthermore, the EIGHT study provided large scale data on Africa and was supported by robust statistical methods where patient adherence was considered. Active involvement of African cardiologists, who are familiar with the problems of this area, helped formulate specific questions and analysis.

Perspectives

In this African setting, in addition to expected factors, drug strategies for controlling elevated BP were associated with country-level income, patient location and finally, the interplay between both in low-income countries. Physicians adapt patients care to country-level income and accessibility to treatment according to patient location. These results highlight the importance of developing policies that seek to make multiple drug classes accessible particularly in rural low-income countries.

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Conflicts of interest

There are no conflicts of interest.

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