Antihypertensive strategies and hypertension control in Sub-Saharan Africa

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High blood pressure(BP) is the main contributor to the global burden of chronic disease reaching 10 million deaths each year(1). In Africa, 130.2 million people suffer from hypertension and this figure is expected to reach 216.8 million by 2030(2). A combination of lifestyle modification and blood pressure-lowering medications are the cornerstone of hypertension control. Even though antihypertensive medications reduce hypertension-related complications, large-scale data on their use in Sub-Saharan Africa(SSA) are scarce(3). Furthermore, most studies in SSA are limited to single countries or centers(4).

We aimed to describe BP control and antihypertensive drug strategies using a large multinational study conducted in 12 SSA countries: the EIGHT Study(Evaluation of Hypertension in Sub-Saharan Africa)(5).

We conducted an observational cross-sectional study using data collected during outpatient consultations for hypertension in cardiology departments of 29 hospitals from 17 cities across 12 SSA countries. The EIGHT study was conceived by a multidisciplinary collaborative team of epidemiologists, cardiologists and pharmacists from Africa and France.

The study was approved by the Ile-de-France III ethics committee(Number_2014-A00710-47) and was exclusively supported by a public grant.

Consecutive men and women ≥18 years of age with hypertension were enrolled at any visit during outpatient consultations in the cardiology departments of the participating hospitals. Hypertension diagnosis was defined according to a BP level≥140/90 mmHg. Seated office BP was measured twice by physicians, at least 15 minutes apart; participants were instructed to avoid caffeine and smoking within 30 minutes prior to BP measurement. Uncontrolled hypertension was defined by a systolic BP(SBP) ≥ 140 mm Hg and/or a diastolic BP(DBP) of ≥90 mmHg of the measured office BP values in the clinic(6). Severity of hypertension was defined according to European Society of Cardiology guidelines(6): SBP:140-159 mmHg and/or DBP:90-99 mmHg, SBP:160-179 mmHg and/or DBP:100-109 mmHg and SBP≥180 mmHg and/or DBP ≥110 mmHg. Antihypertensive drugs classes were reported by the physician during the consultation.

Continuous and categorical variables were expressed as mean(standard deviation) and numbers(percentage) where appropriate. Categorical variables were compared using Chi-square tests. A two tailed p value of <0.05 was considered significant. Analyses were performed with R software(version 3.5.1(2018-07-02)).

A total of 2198 hypertensive patients (58.4±11.8years; 39.9% male) were included from six low-income countries(Benin, Democratic Republic of the Congo, Guinea, Mozambique, Niger and Togo) and six middle-income countries(Cameroon, Congo(Brazzaville), Gabon, Côte d'Ivoire, Mauritania, Senegal). Among whom 2123(96.6%) had at least one antihypertensive drug, ranged from 88.8% in Niger and Senegal to 100% in Mauritania and Mozambic(Table 1).

The use of a monotherapy ranged from 13.5% in Togo to 48.2% in Democratic Republic of the Congo. The use of two-drug strategies ranged from 31.8% in Mozambic to 52.4% in Guinea. Three- and more drug strategies varied from 2.9% in Guinea to 44.2% in Togo. The proportion of drugs strategies differed significantly according to countries($p<0.001$). Furthermore, we observed a significant difference of strategies between low- and middle-income countries(55.3% and 44.7% of monotherapy, respectively; $p<0.001$). In addition, in low income countries monotherapy was prescribed more than two or three- and more drug strategies($p<0.001$) whereas in middle income countries, three- and more drug strategies were more frequently prescribed than monotherapy or two-drug strategies $p<0.001$).

Among patients prescribed antihypertensive medication, mean systolic BP was 148.9±23.4mmHg and mean of diastolic BP measures was 88.2±14.2mmHg(Table1). Indeed, 1630(76.7%) had uncontrolled BP(range: 57.1%(140/245) in Benin to 100%(89/89) in Gabon, Figure 1). Among patients taking antihypertensive medication with uncontrolled hypertension (n=1630), 625(38.3%), 543(33.3%) and 462(28.3%) patients had hypertension ≥140/90mmHg, ≥160/100mmHg and ≥180/110mmHg respectively(Table 1). The percentage of patients with hypertension ≥180/110mmHg varied from 16.2%(20/123) in Guinea to 58.7%(47/80) in Gabon. Among patients with hypertension ≥180/110mmHg, 127(27.5%) were treated with a monotherapy. This proportion varied from 5.9% in Niger to 53% in Democratic Republic of the Congo.

In discussion, antihypertensive drug strategies differed largely according to country. The proportion of monotherapy in Democratic Republic of the Congo was three times higher than in Togo where the proportion of three- and more drug strategies was fifteen times higher than that of Guinea. In contrast, Guinea was the country where the proportion of two-drug strategies is the highest.

Furthermore, hypertension is poorly controlled in this region even among those who are taking medications. A high proportion(28.3%) of patients with uncontrolled BP had hypertension ≥180/110mmHg, of whom 27.5% were still treated with a monotherapy. Our results are in keeping with the results collected in different regions of the world. Primary prevention efforts are poorly developed in people with high cardiovascular risk(7,8). According to international guideline(6), these patients should be uptitrated with double, triple or more combination therapy(9). The high proportion of patients with hypertension ≥180/110mmHg who were only treated with a monotherapy may be due not only to physicians' lack of knowledge of guidelines but, may be also due to clinical inertia, patient socioeconomic factors and behavior, or availability and affordability of antihypertensive medications. However, even though combination therapy is known to improve BP control(9), the proportion of uncontrolled hypertension remained very high even in patients who were prescribed combination therapy. We cannot exclude that the pharmaceutical quality of drugs did not contribute to treatment failure. Indeed, we have previously shown in the SEVEN study that 16% of cardiovascular drugs have

poor quality in SSA especially CCBs, and the proportion of poor quality can reach 50% when drugs produced in Asia are sold in street markets(10).

We acknowledged the following limitations. The sampling framework in each country was not nationally representative, and therefore caution is needed in extrapolating the information in the current study to other populations.

Our study had many strengths including its multisite design, with over 2000 patients from 29 medical centers in 17 cities from 12 countries. Our analysis provided the opportunity to extend knowledge on effectiveness of antihypertensive strategies in the African continent.

In conclusion, our study described antihypertensive drug strategies prescribed in 12 Sub-Saharan countries. Even among patients recruited from tertiary cardiology centers in urban areas in Sub-Saharan countries and prescribed antihypertensive medications for almost all of them, BP control remains very poor and there is a large room for improvement in medical treatment.

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Author's contribution:

All authors have substantial contributions.

M. Antignac and X. Jouven had full access to the whole data in the study and take responsibility for integrity of the data and accuracy of data analysis. They take responsibility for all aspects of the reliability and freedom from bias of presented data and their discussed interpretation.

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References

1. GBD 2017 Risk Factor Collaborators. Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet Lond Engl. 2018 10;392(10159):1923–94.

2. Adeloye D, Basquill C. Estimating the prevalence and awareness rates of hypertension in Africa: a systematic analysis. PloS One. 2014;9(8):e104300.

3. Attaei MW, Khatib R, McKee M, Lear S, Dagenais G, Igumbor EU, et al. Availability and affordability of blood pressure-lowering medicines and the effect on blood pressure control in high-income, middle-income, and low-income countries: an analysis of the PURE study data. Lancet Public Health. 2017;2(9):e411–9.

4. Mutua EM, Gitonga MM, Mbuthia B, Muiruri N, Cheptum JJ, Maingi T. Level of blood pressure control among hypertensive patients on follow-up in a regional referral hospital in Central Kenya. Pan Afr Med J. 2014;18:278.

5. Antignac M, Diop IB, Macquart de Terline D, Kramoh KE, Balde DM, Dzudie A, et al. Socioeconomic Status and Hypertension Control in Sub-Saharan Africa: The Multination EIGHT Study (Evaluation of Hypertension in Sub-Saharan Africa). Hypertension. 2018 Apr;71(4):577–84.

6. ESH/ESC Task Force for the Management of Arterial Hypertension. 2013 Practice guidelines for the management of arterial hypertension of the European Society of Hypertension (ESH) and the European Society of Cardiology (ESC): ESH/ESC Task Force for the Management of Arterial Hypertension. J Hypertens. 2013 Oct;31(10):1925–38.

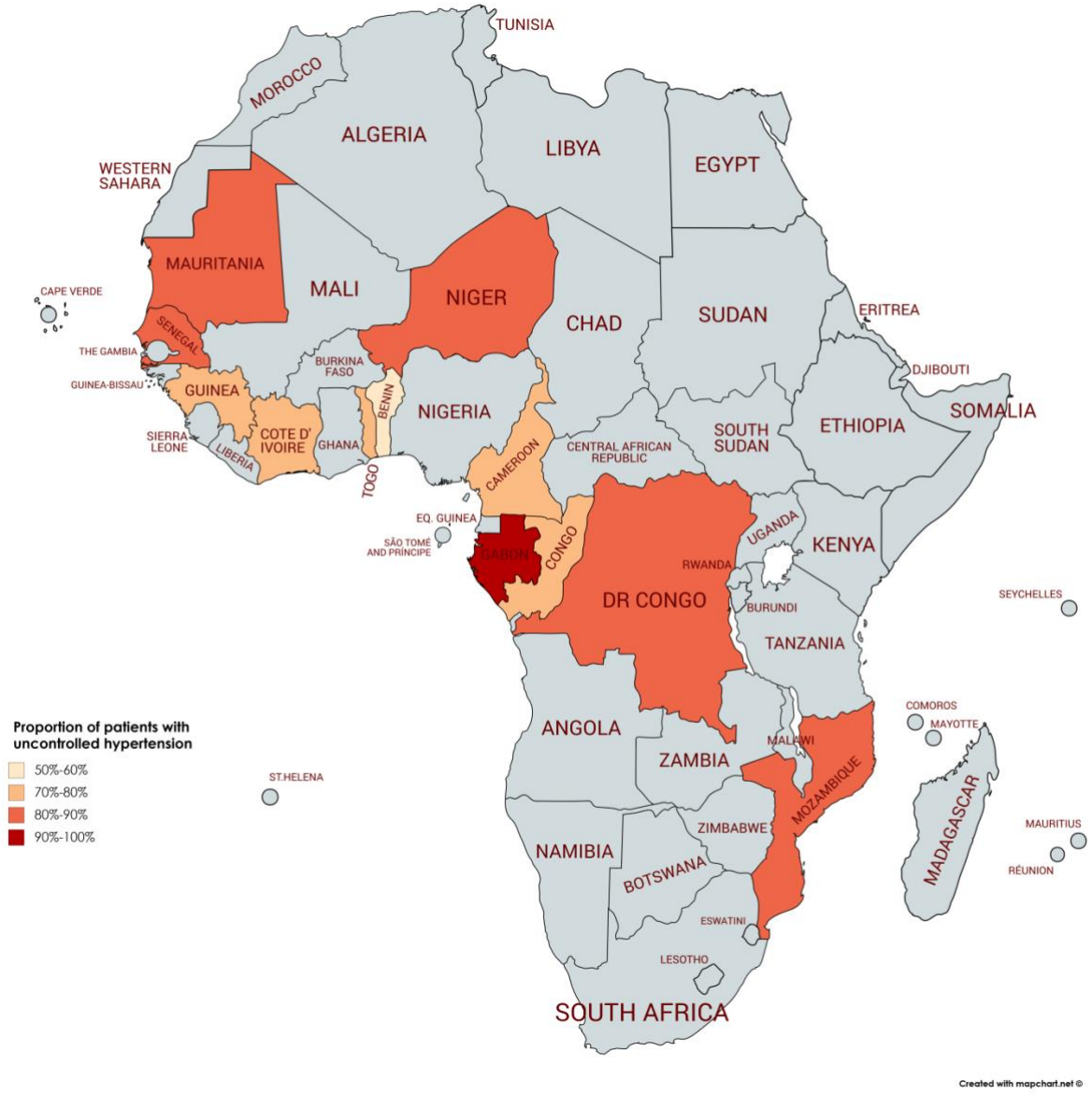
7. Kotseva K, De Backer G, De Bacquer D, Rydén L, Hoes A, Grobbee D, et al. Lifestyle and impact on cardiovascular risk factor control in coronary patients across 27 countries: Results from the European Society of Cardiology ESC-EORP EUROASPIRE V registry. Eur J Prev Cardiol. 2019;26(8):824–35.

8. Kotseva K, De Backer G, De Bacquer D, Rydén L, Hoes A, Grobbee D, et al. Primary prevention efforts are poorly developed in people at high cardiovascular risk: A report from the European Society of Cardiology EURObservational Research Programme EUROASPIRE V survey in 16 European countries. Eur J Prev Cardiol. 2020 Mar 20;2047487320908698.

9. Ojji DB, Mayosi B, Francis V, Badri M, Cornelius V, Smythe W, et al. Comparison of Dual Therapies for Lowering Blood Pressure in Black Africans. N Engl J Med. 2019 Mar;

10. Antignac M, Diop BI, Macquart de Terline D, Bernard M, Do B, Ikama SM, et al. Fighting fake medicines: First quality evaluation of cardiac drugs in Africa. Int J Cardiol. 2017 Sep 15;243:523–8.

Figure 1: Proportion of patients with uncontrolled hypertension



Legend: Grey countries were not included in the EIGHT study.

Table 1: Treated patients characteristics by country

	GLOBAL	Niger	Togo	Benin	Guinea	Mozambic	Dem. Rep of the Congo	Congo	Senegal	Côte d'Ivoire	Cameroon	Mauritania	Gabon
N, (%)	2198	80 (3.6)	106 (4.8)	250 (11.4)	172 (7.8)	148 (6.7)	261 (11.9)	178 (8.1)	160 (7.3)	295 (13.5)	375 (17.1)	84 (3.8)	89 (4)
Age (year), mean (sd)	58.3 (11.8)	56.6 (11.9)	55.7 (10.6)	56 (12.6)	57.8 (8)	53.4 (11.2)	62.5 (11.1)	55.9 (11.9)	58.9 (12.5)	60.1 (11.5)	60.9 (12.1)	57.1 (9.5)	53.7 (11.9)
Male, N (%)	874 (39.8)	34 (42.5)	44 (41.5)	91 (36.4)	114 (66.3)	71 (48.0)	89 (34.1)	63 (35.4)	50 (31.2)	135 (45.8)	126 (33.6)	32 (38.1)	25 (28.1)
Patients on antihypertensive medication, N (%)	2123 (96.6)	71 (88.8)	104 (98.1)	246 (98.4)	170 (98.8)	148 (100)	255 (97.7)	177 (99.4)	142 (88.8)	292 (99)	354 (94.4)	84 (100)	80 (89.9)
Antihypertensive drug class, N (%)													
Calcium channel blocker	1219 (57.4)	38 (53.5)	67 (64.4)	176 (71.5)	54 (31.8)	114 (77.0)	146 (57.3)	93 (52.5)	74 (52.1)	159 (54.5)	208 (58.8)	51 (60.7)	39 (48.8)
Diuretic	1167 (55.0)	54 (76.1)	71 (68.3)	97 (39.4)	85 (50.0)	70 (47.3)	145 (56.9)	125 (70.6)	80 (56.3)	130 (44.5)	225 (63.6)	30 (35.7)	55 (68.8)
RAS Blocker : Angiotensin-converting-enzyme inhibitor	981 (46.2)	50 (70.4)	69 (66.3)	95 (38.6)	91 (53.5)	14 (9.5)	100 (39.2)	109 (61.6)	77 (54.2)	141 (48.3)	191 (54.0)	13 (15.5)	31 (38.8)
RAS Blocker : Angiotensin II receptor antagonist	321 (15.1)	2 (2.8)	17 (16.3)	60 (24.4)	2 (1.2)	37 (25.0)	4 (1.6)	37 (20.9)	15 (10.6)	70 (24.0)	20 (5.6)	47 (56.0)	10 (12.5)
Beta-blocker	466 (22.0)	12 (16.9)	36 (34.6)	45 (18.3)	37 (21.8)	30 (20.3)	25 (9.8)	51 (28.8)	41 (28.9)	86 (29.5)	70 (19.8)	31 (36.9)	2 (2.5)
Centrally active drug	79 (3.7)	2 (2.8)	4 (3.8)	14 (5.7)	0 (0.0)	11 (7.4)	15 (5.9)	1 (0.6)	5 (3.5)	11 (3.8)	10 (2.8)	0 (0.0)	6 (7.5)
Vasodilator	33 (1.6)	7 (9.9)	0 (0.0)	1 (0.4)	0 (0.0)	3 (2.0)	0 (0.0)	1 (0.6)	4 (2.8)	12 (4.1)	1 (0.3)	0 (0.0)	4 (5.0)
Office Blood pressure, mean (sd)													
Systolic blood pressure, mmHg	148.9 (23.4)	153.9 (25.1)	142.7 (20.2)	139.3 (22.5)	139.9 (17.5)	144.1 (19.8)	150.01 (22.5)	148.5 (20.5)	146.9 (22.5)	155.8 (25.7)	151.4 (23.4)	149.4(22.2)	175.6 (21.2)
Diastolic blood pressure, mmHg	88.2 (14.2)	91.8 (13.8)	86.9 (14.6)	84.3 (13.3)	87.6 (10.2)	91.4 (13.8)	91.0 (15.2)	87.1 (12.3)	90.4 (13.4)	84.7 (15.1)	87.1 (14.1)	87.8 (11.8)	104.5 (13.4)
Blood pressure control* (Uncontrolled vs controlled), N (%)	1630 (76.7)	65 (84.4)	77 (72.6)	142 (57)	125 (73.5)	119 (80.4)	232 (89.2)	134 (75.3)	128 (80.5)	228 (77.8)	285 (76.6)	68 (81)	89 (100)
NA	10	3	0	1	2	0	1	0	1	2	3	0	0
Hypertension severity, N (%)													
Grade 1	625 (38.3)	15 (23.1)	40 (51.9)	51 (35.9)	70 (56.0)	31 (26.1)	86 (37.1)	70 (52.2)	50 (39.1)	77 (33.8)	115 (40.4)	35 (51.5)	8 (9.0)
Grade 2	543 (33.3)	31 (47.7)	22 (28.6)	59 (41.5)	35 (28.0)	47 (39.5)	69 (29.7)	38 (28.4)	49 (38.3)	87 (38.2)	77 (27.0)	16 (23.5)	28 (31.5)
Grade 3	462 (28.3)	19 (29.2)	15 (19.5)	32 (22.5)	20 (16.0)	41 (34.5)	77 (33.2)	26 (19.4)	29 (22.7)	64 (28.1)	93 (32.6)	17 (25.0)	53 (59.6)

***** Uncontrolled hypertension was defined by a systolic BP (SBP) ≥ 140 mm Hg and/or a diastolic BP (DBP) of ≥90 mmHg on either of office BP measures in the clinic.