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## Poor adherence to medication and salt restriction as a barrier to reaching blood pressure control in patients with hypertension: Cross-sectional study from 12 sub-Saharan countries

**Abbreviated title:** Adherence and blood pressure control in sub-Saharan Africa

**Diane Macquart de Terline<sup>a,b,c,\*</sup>, Kouadio Euloge Kramoh<sup>d</sup>, Ibrahima Bara Diop<sup>e</sup>, Carol Nhavoto<sup>f</sup>, Dadhi M. Balde<sup>g</sup>, Beatriz Ferreira<sup>f</sup>, Martin Dèdonougbo Houenassi<sup>h</sup>, Dominique Hounsou<sup>h</sup>, Méo Stéphane Ikama<sup>i</sup>, Adama Kane<sup>j</sup>, Suzy Gisèle Kimbally-Kaki<sup>i</sup>, Samuel Kingue<sup>k</sup>, Florent Koffi<sup>d</sup>, Charles Kouam Kouam<sup>l</sup>, Emmanuel Limbole<sup>m</sup>, Liliane Mfeukeu Kuate<sup>n</sup>, Jean Bruno Mipinda<sup>o</sup>, Yves N'goran<sup>d</sup>, Zouwera Sesso<sup>p</sup>, Abdallahi Sidy Ali<sup>q</sup>, Ibrahim Ali Toure<sup>r</sup>, Pierre François Plouin<sup>b,c,s</sup>, Michel Azizi<sup>b,c,s</sup>, Marie Cécile Perier<sup>b</sup>, Kumar Narayanan<sup>t</sup>, Jean Philippe Empana<sup>b</sup>, Xavier Jouven<sup>b,c,s</sup>, Marie Antignac<sup>a,b</sup>**

<sup>a</sup> *Department of Pharmacy, Saint-Antoine Hospital, HUEP, AP-HP, 75012 Paris, France*

<sup>b</sup> *Paris Cardiovascular Research Centre, INSERM U970, Georges-Pompidou European Hospital, 75015 Paris, France*

<sup>c</sup> *Paris Descartes University, 75006 Paris, France*

<sup>d</sup> *Institute of Cardiology of Abidjan, BPV 206 Abidjan, Côte d'Ivoire*

<sup>e</sup> *Cardiology Department, University Hospital of Fann, Dakar, Senegal*

<sup>f</sup> *Instituto do Coração (ICOR), Maputo, Mozambique*

<sup>g</sup> *Department of Cardiology, University Hospital of Conakry, Guinea*

<sup>h</sup> *National University Hospital of Hubert K. Maga (CNHU-HKM), 01 BP 386 Cotonou, Bénin*

<sup>i</sup> *Cardiology Department, National University Hospital of Brazzaville, Marien Ngouabi University, Brazzaville, Congo*

<sup>j</sup> *Cardiology Department, University Hospital of Aristide Le Dantec, Dakar, Senegal*

<sup>k</sup> *University of Yaoundé, Ministry of Public Health, Cameroon*

<sup>l</sup> *Internal Medicine Department, Regional Hospital, Bafoussam, Cameroon*

<sup>m</sup> *Department of Internal Medicine of la Gombe (CMCG), Ngaliema Hospital, Kinshasa, Democratic Republic of the Congo*

<sup>n</sup> *Central Hospital of Yaoundé, Cameroon*

<sup>o</sup> *University Hospital of Libreville, Libreville, Gabon*

<sup>p</sup> *Cardiology Department, Lomé, Togo*

<sup>q</sup> *Cardiology Clinics, Nouakchott, Mauritania*

<sup>r</sup> *Internal Medicine and Cardiology Departement, University Hospital of Lamordé, Niamey University, Niamey, Niger*

<sup>s</sup> *Department of Cardiology, Georges-Pompidou European Hospital, AP-HP, 75015 Paris, France*

<sup>t</sup> *MaxCure Hospitals, Hyderabad, Telangana 500081, India*

\* Corresponding author at: Hôpital Saint-Antoine, AP-HP, 184 rue du Faubourg Saint-Antoine, 75012 Paris, France.

*E-mail address:* [diane.macquart-de-terline@aphp.fr](mailto:diane.macquart-de-terline@aphp.fr); [diane.de.terline@gmail.com](mailto:diane.de.terline@gmail.com) (D. Macquart de Terline).

## **Summary**

*Background.* – Sub-Saharan Africa is experiencing a rising burden of hypertension. Antihypertensive medications and diet are the cornerstone of effective hypertension control.

*Aims.* – To assess adherence to medication and salt restriction in 12 sub-Saharan countries, and to study the relationship between adherence and blood pressure control in patients with hypertension.

*Methods.* – We conducted a cross-sectional survey in urban clinics in twelve sub-Saharan countries. Data were collected on demographics, treatment and adequacy of blood pressure control in patients with hypertension attending the clinics. Adherence was assessed by questionnaires completed by the patients. Hypertension grades were defined according to European Society of Cardiology guidelines. Association between adherence and blood pressure control was investigated using multilevel logistic regression analysis, adjusting for age, sex and country.

*Results.* – Among the 2198 patients, 77.4% had uncontrolled blood pressure, 34.0% were poorly adherent to salt restriction, 64.4% were poorly adherent to medication and 24.6% were poorly adherent to both. Poor adherence to salt restriction (odds ratio [OR] 1.33, 95% confidence interval [CI] 1.03–1.72), medication (OR 1.56, 95% CI 1.25–1.93) or both (OR 1.91 1.39–2.66) was related to uncontrolled blood pressure. Moreover, poor adherence to both medication and salt restriction was related to a 1.52-fold (95% CI 1.04–2.22), 1.8-fold (95% CI 1.22–2.65) and 3.08-fold (95% CI 2.02–4.69) increased likelihood of hypertension grade 1, 2 and 3, respectively.

*Conclusions.* – High levels of poor adherence to salt restriction and medication were noted in this urban sub-Saharan study; both were significantly associated with uncontrolled blood pressure, representing major opportunities for intervention to improve hypertension control in sub-Saharan Africa.

## **KEYWORDS**

Hypertension;

Epidemiology;

Global health;

Medication adherence;

Sub-Saharan Africa

*Abbreviations:* BP, blood pressure; CI: confidence interval; OR: odds ratio.

## **Background**

Over the next decade, the number of adults with hypertension is predicted to increase by about 60%, reaching a total of 1.56 billion in 2025, with a disproportionately high burden in developing countries, including sub-Saharan Africa [1]. In 2008, the African region already had the highest prevalence rate, i.e. 46% in adults aged  $\geq 25$  years [2]. More concerning, this region has one of the least developed health systems in the world [3]. Numerous reports and studies over the years have indicated that the prevention, detection, management and control of high blood pressure (BP) are haphazard and insufficient [4]. It is estimated that if patients with hypertension in sub-Saharan Africa were treated effectively, about 250,000 deaths would be prevented annually [5]. Tackling the burden of hypertension in sub-Saharan Africa should therefore be regarded as a high-priority task.

Antihypertensive medications to lower BP in patients with hypertension substantially decrease their risk of adverse cardiovascular outcomes [6, 7]. Simultaneously, worldwide, estimates suggest that 1.65 million deaths from cardiovascular causes that occurred in 2010 were attributable to sodium consumption above a reference level of 2.0 g per day [8]. Unfortunately, adherence to antihypertensive treatment and diet modifications are often below optimum.

Previous studies have highlighted the importance of patient adherence to antihypertensive therapy in order to achieve BP control and successful primary prevention of cardiovascular events [9, 10]. Indeed, poor adherence to medication is a leading reason for poor BP control among patients treated for hypertension [6, 10]. Concerning diet modification, there is strong evidence that reduction in salt intake reduces BP [8], and that black people are more sensitive to the beneficial effect of salt reduction [11]. Therefore, strategies to enhance patient adherence to medication and lifestyle modification are effective ways to reduce the burden of hypertension.

Overall, limited data exist with regard to adherence to both antihypertensive medication and salt restriction, and there are even fewer data in resource-poor regions. We therefore performed a study to assess adherence to salt restriction and medication, and to study the association with BP control, in patients with hypertension in 12 sub-Saharan African countries.

## **Methods**

### **Study design and setting**

We conducted an observational cross-sectional study during outpatient consultations in the cardiology

departments of 29 medical centres from 17 cities across 12 sub-Saharan African countries (Bénin, Cameroon, Congo [Brazzaville], Democratic Republic of the Congo, Gabon, Guinea, Côte d'Ivoire, Mauritania, Mozambique, Niger, Senegal and Togo) between January 2014 and November 2015.

The study was conceived and designed by a multidisciplinary collaborative team of epidemiologists, cardiologists and pharmacists from Africa and France. The team had extensive previous research experience, and existing collaborations with a network of physician-scientists in Africa, in fields such as rheumatic heart disease [12-15], sickle cell disease [16, 17] and quality of cardiovascular drugs [18, 19], which helped with the planning and launch of the present study.

Informed consent was obtained from each patient. 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).

## **Participants**

Patients were enrolled during outpatient consultations in the cardiology departments of the participating hospitals. Patients aged  $\geq 18$  years with a diagnosis of hypertension were eligible to participate. 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 the eligibility criteria. Patients who agreed to participate completed a standard questionnaire while waiting for their appointment. Participating investigators (physicians) at each centre received a training note detailing the study, with standardized instructions on how they should interact with the patients while completing the questionnaire.

## **Questionnaire and measurements**

### **Questionnaire**

The questionnaire was conceived by the authors of the study, and included two major sections. The first section was completed by patients, and collected data on patient demographics (age, sex, marital status, etc.), individual salt consumption and adherence to treatment. The second section was filled out by the physician during the consultation, and collected data on the patient's socioeconomic status, drug regimen, clinical data, BP values (measured in standardized conditions; see below) and

cardiovascular risk factors.

## **Patient and public involvement**

A pilot investigation involving 90 patients who tested the questionnaire was conducted in January 2014 in Côte d'Ivoire. This pilot study confirmed patient understanding and feasibility of completion, and resulted in a few modifications that were incorporated into the questionnaire given to the patients in the final survey.

## **Salt consumption and adherence to salt restriction**

Salt consumption was evaluated by questionnaire items related to behaviour regarding salt restriction recommendations, salt addition to dishes (during and after preparation) and consumption of salted food.

Adherence to salt restriction was assessed based on answers related to the frequency of salt addition to meals and consumption of salted food (three items). Each item was rated as 0 (less than twice a week), 1 (twice a week) or 2 (more than twice a week), yielding a score of adherence to salt restriction ranging from 0 to 6. In the main analysis, a score  $\geq 3$  defined poor adherence to salt restriction. The original score was also investigated in the sensitivity analysis.

## **Adherence to medication**

Adherence to medication was assessed by the eight-item Medication Adherence Scale, each item being categorized as yes/no, yielding a score ranging from 0 to 8 [20]. In the main analysis, poor adherence to medication was defined as a score of strictly  $< 8$  on the Medication Adherence Scale. In the sensitivity analyses, adherence to medication was categorized using three cut-off points published previously [20] (a score of  $< 6$  indicates low adherence, 6 to 8 indicates medium adherence and 8 indicates high adherence). We also used adherence score as a discrete variable ranging from 0 to 8 to assess the association between adherence and BP control.

## **Adherence to both salt restriction and medication**

Combining information on both adherence to salt restriction and medication, patients were categorized into four groups: good adherents (good adherence to both salt restriction and medication); discordant



adherents (two groups: poor adherence to salt restriction and good adherence to medication; or good adherence to salt restriction and poor adherence to medication); and poor adherents (poor adherence to both salt restriction and medication).

## **BP measurement**

Sitting BP was measured twice by physicians, at least 15 minutes apart; attention was paid to avoid caffeine and smoking during the 30 minutes before the BP measurement.

Uncontrolled hypertension was defined by a systolic BP  $\geq 140$  mmHg and/or a diastolic BP  $\geq 90$  mmHg on either of the measured BP values in the clinic [21].

Stages of hypertension were defined according to European Society of Cardiology guidelines [22]: grade 1 hypertension (systolic BP 140–159 mmHg and/or diastolic BP 90–99 mmHg); grade 2 hypertension (systolic BP 160–179 mmHg and/or diastolic BP 100–109 mmHg); and grade 3 hypertension (systolic BP  $\geq 180$  mmHg and/or diastolic BP  $\geq 110$  mmHg).

## **Statistical methods**

Continuous and categorical variables are expressed as means  $\pm$  standard deviation and numbers (percentages), as appropriate. The characteristics of the study participants were compared according to their adherence category using logistic regression, adjusting for country.

First, logistic regression models were used to quantify the association between uncontrolled BP and poor adherence, using good adherence as the reference category. Then, polytomous logistic regressions were used to quantify the association between hypertension grades and poor adherence categories, using good adherence as the reference category.

All regression models were adjusted for age, sex and country. All analyses were performed through scripts developed in R software, (version 3.2.3). The level of significance was set at  $P < 0.05$ .

## **Results**

### **Participants**

We enrolled 2198 individuals in 12 sub-Saharan countries between January 2014 and November 2015. Patients' baseline data are reported in [Table 1](#); 60.2% were women, and the mean age was  $57.7 \pm 12.0$  years for women and  $59.2 \pm 11.4$  years for men. Among participants, 41.6% had a low

education level (no education or primary education), 33.3% had a medium level (secondary school) and 25.1% had a high level (tertiary or above). The majority of patients were living in an urban setting ( $n = 1702$ , 78.9%).

Most patients ( $n = 1816$ , 84.4%) had been diagnosed with hypertension for more than a year. During the consultation, 1692 patients (77.4%) had uncontrolled BP. A total of 648 (38.3%), 558 (33.0%) and 486 (28.7%) patients had grade 1, 2 and 3 hypertension, respectively. Overall, 2094 participants were aware of their condition (95.3%; 95% confidence interval [CI] 94.3–96.1%), and 2123 were receiving at least one antihypertensive medication (96.6%; 95% CI 95.7–97.3%). Data by country are presented in [Table A.1](#).

## **Salt consumption and adherence to salt restriction**

A total of 1841 (85.6%) patients acknowledged having received instruction from their doctor to reduce salt intake, and 82.5% declared that they had decreased their salt intake since the hypertension diagnosis. Most patients ( $n = 1355$ , 62.3%) declared that their salt consumption was low.

Nevertheless, 63.6% conceded not being in charge of cooking meals at home (43.4% of women and 94.0% of men), implying that they were probably unaware of the precise amount of salt added to their food.

Overall, 34.0% of patients were considered to be poorly adherent to salt restriction. Poor adherence to salt restriction differed significantly ( $P < 0.001$ ) according to country, reaching 73.8% in Côte d'Ivoire ([Fig. 1A](#)). Poor adherence to salt restriction was more likely among younger patients, with a greater education level, a more recent diagnosis of hypertension, fewer antihypertensive treatments and a higher body mass index compared with good adherence ([Table 1](#)).

## **Adherence to medication**

In the study population, 64.4% of participants had poor adherence to medication. The proportion of poor adherents to medication differed significantly by country ( $P < 0.001$ ), ranging from 47.1% in Guinea to 80.5% in the Democratic Republic of the Congo ([Fig. 1B](#)). Those who were poorly adherent to medication were more likely to have fewer antihypertensive medications compared with those who had good adherence ([Table 1](#)).

## **Adherence to both salt restriction and medication**

Overall, 24.6% (95% CI 22.8–26.5) of the participants were poor adherents to both salt restriction and medication. Almost half of the patients, 48.8% (95% CI, 46.6–50.9) had a discordant adherence profile, with either poor adherence to salt restriction and good adherence to medication (9.4%, 95% CI 8.1–10.7) or good adherence to salt restriction and poor adherence to medication (39.4%, 95% CI 37.3–41.5). Good adherence to both salt restriction and medication was seen in 26.6% (95% CI 24.7–28.6) of the participants.

## **Association of adherence to salt restriction, medication and both with BP control**

Poor adherence to salt restriction (odds ratio [OR] 1.33, 95% CI 1.03–1.72) or to medication (OR 1.56, 95% CI 1.25–1.93) was significantly associated with uncontrolled BP ([Table 2](#)).

Even in patients who were adherent to both medication and salt restriction, the proportion with uncontrolled BP reached 70.4%. This proportion increased as adherence to salt restriction and to medication declined: 77.5%, 79.3% and 81.2%, respectively, in patients with poor adherence to salt restriction and good adherence to medication, those with good adherence to salt restriction and poor adherence to medication and those with poor adherence to both medication and salt restriction ( $P < 0.001$ ). Associated ORs are reported in [Table 2](#). Further adjustment for body mass index did not change these results.

## **Association of adherence to salt restriction, medication and both with hypertension severity**

Poor adherence (to salt restriction, medication or both) was also associated with a higher stage of hypertension ([Fig. 2](#)). For instance, the likelihood of having grade 1, 2 or 3 hypertension increased 1.52 fold (95% CI 1.04–2.22), 1.8 fold (95% CI 1.22–2.65) and 3.08 fold (95% CI 2.02–4.69), respectively, in patients who were poorly adherent to both salt and medication restriction compared with those who adhered well to both.

## Sensitivity analysis

First, when considering the score of adherence to salt restriction (ranging from 0 to 6, the likelihood of uncontrolled BP increased 1.14 fold per additional point in the score (OR 1.14, 95% CI 1.03–1.27;  $P = 0.013$ ).

Second, when considering the score of adherence to medication, the likelihood of uncontrolled BP increased 1.18 fold per additional point in the score (OR 1.18, 95% CI 1.11–1.25). In addition, when considering three levels of adherence to medication (< 6, 6–8 and 8, representing low, medium and high levels of adherence, respectively), patients with medium adherence to medication (OR 1.32, 95% CI 1.04–1.69;  $P = 0.025$ ) and low adherence to medication (OR 1.92, 95% CI 1.47–2.53;  $P < 0.001$ ) were more likely to have uncontrolled BP.

## Discussion

Our study is the first multinational report on adherence and uncontrolled hypertension from sub-Saharan Africa, covering 2198 patients. We investigated the specific associations between poor adherence to pharmacological and non-pharmacological (salt restriction) treatment and achievement of adequate hypertension control. Our results underline the considerably high proportion of poorly adherent patients: more than two-thirds of patients were poorly adherent to medication, more than one third were poorly adherent to salt restriction and a quarter were poorly adherent to both. We also highlighted the strikingly high proportion of patients with uncontrolled BP (77.4%). The proportion of patients with uncontrolled BP varied significantly according to the adherence level, and was significantly associated with poor adherence to salt restriction and to medication (respective ORs 1.33 and 1.56). When combining poor adherence to both salt restriction and medication, the OR for uncontrolled BP was 1.91. Furthermore, poor adherence was related to hypertension severity, with a 1.52-fold, 1.8-fold and 3.08-fold increased likelihood of hypertension grade 1, 2 and 3, respectively, in poor adherents to both salt restriction and medication.

In resource-limited countries, medication adherence has received very little attention. Even the World Health Organization report [23] that highlights the global problem of non-adherence relies almost exclusively on study data from the developed world.

Given the scarcity of health resources available in developing countries, only quality improvement interventions that are cost-efficient are likely to be feasible [24]. Improved adherence may provide an

opportunity not only to improve cardiovascular outcomes, but also to reduce healthcare spending [23, 25, 26]. A systematic review of intervention to improve adherence [27] stated that “effective ways to help people follow medical treatments could have far larger effects on health than any treatment itself”. Our results showed a high proportion of poorly adherent patients (34.0% to salt restriction, 64.4% to medication), suggesting considerable leverage to improve the situation.

There are several effective ways to improve adherence in patients with hypertension. First, interventions targeting patients should be considered. For example, a randomized controlled trial showed that a pharmacy care programme led to increases in medication adherence and medication persistence, and clinically meaningful reductions in BP, when compared with usual care [28]. Also, recent technological advances, such as mobile phone text messages [29] and smartphone adherence apps [30, 31], have now been developed to support treatment adherence in adults with high BP. Second, interventions should not only focus on patients. Indeed, patients will be more likely to take their drugs if health professionals are knowledgeable about and have skills in improving adherence. Education of health professionals should be planned in order to achieve this goal [32]. Third, this matter should be addressed at national level. Global health strategies should incorporate population-wide measures, especially promotion of salt reduction policies. At present, interventions recommended by the World Health Organization, such as reformulation of processed foods, consumer awareness and environmental changes to increase the availability and affordability of healthy food, are lacking in sub-Saharan Africa [33].

Our results demonstrate the high proportion of uncontrolled BP in sub-Saharan countries. Tackling the burden of hypertension in developing countries presents a global challenge to healthcare providers, researchers, government officials and the general public to develop and implement effective clinical and public health strategies that lead to sustained changes. Among these, raising detection, diagnosis and awareness [34] of raised BP, improving the availability, affordability [35] and quality of hypertensive treatments [36] and enhancing adherence to medication and diet modifications, should be part of the global plan.

## **Study limitations and strengths**

One of the limitations to our study is that the sampling framework in each country was not nationally representative, and therefore caution is needed in extrapolating the information as being

representative of the status in each country. Although a random selection of centres from African countries would be ideal from a methodological perspective, such an approach is impractical, given the lack of cardiovascular care in this part of the world.

Moreover, another limitation that should be acknowledged is the way that adherence to salt restriction was assessed. Methods such as measures of urinary sodium and dietary recalls are effective ways to assess salt consumption. However, these methods are either expensive or hardly usable during a consultation, and therefore could not be used in the setting of this study. We chose a cut-off of  $\leq 3$  corresponding to clinically relevant information regarding the addition of salt during meals. This choice is questionable, and the proportion of poorly adherent patients (34.0%) is directly related to the threshold value. In addition, the proportion of poor adherence to salt restriction is probably much higher than that observed. Indeed, 63.6% conceded that they were not in charge of cooking meals at home (43.4% of women and 94.0% of men), implying that they are unaware of the precise amount of salt taken during their meals. Therefore, in the study, adherence to salt restriction was measured by a score based on answers to salt addition to meals and consumption of salted food, but did not include a question on salt addition during dish preparation. Even if the choice of the cut-off point can be criticized, choosing a cut-off point allowed us to focus on a specific group of patients at greater risk of having uncontrolled BP. However, sensitivity analyses (using the discrete scale) indicate that the association between uncontrolled BP and salt consumption was consistent.

This study also has many strengths, in particular the large number of participating countries and patients, on a scale that is often difficult to achieve in the developing world. Furthermore, our study was supported by a strong and structured collaborative multidisciplinary network. Active involvement of African cardiologists, who are familiar with the problems of this area, helped with derivation of specific questions and analysis.

## **Conclusions**

Poor adherence to either salt restriction or medication or both was significantly associated with uncontrolled BP. These data suggest that improving adherence to antihypertensive medication, in conjunction with diet modifications, should be part of an overall strategy to tackle the burden of hypertension in sub-Saharan Africa.

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### **Disclosure of interest**

The authors declare that they have no conflicts of interest concerning this article..

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## Figure legends

**Figure 1.** A. Poor adherence to salt restriction. B. Poor adherence to medication.

**Figure 2.** Odds ratios (ORs) for hypertension grades according to adherence level to salt restriction or medication. ORs were estimated by polytomous logistic regression, adjusted for age, sex and country, using good adherence as the reference category. CI: confidence interval.

\*N correspond to the number of patients with poor adherence

**Table 1** Characteristics of the participants according to their adherence to salt restriction and medication.

	Global (n = 2198)	Adherence to salt restriction			Adherence to medication		
		Good (n = 1361)	Poor (n = 700)	<i>P</i> <sup>a</sup>	Good (n = 782)	Poor (n = 1416)	<i>P</i> <sup>a</sup>
Age (years)	58.3 ± 11.8	58.8 ± 11.7	57.0 ± 11.9	0.011	58.4 ± 11.3	58.2 ± 12.1	0.18
Male sex	874 (39.8)	531 (39.0)	295 (42.1)	0.08	317 (40.5)	557 (39.3)	0.77
Education level				0.008			0.23
No education	386 (17.9)	229 (17.2)	124 (17.9)		138 (17.9)	248 (17.9)	
Primary	511 (23.7)	324 (24.3)	150 (21.7)		170 (22.1)	341 (24.6)	
Secondary	719 (33.3)	467 (35.0)	202 (29.2)		249 (32.4)	470 (33.8)	
Tertiary or above	542 (25.1)	314 (23.5)	215 (31.1)		212 (27.6)	330 (23.8)	
Urban location (versus rural)	1702 (78.9)	1039 (77.8)	564 (82.1)	0.22	625 (81.1)	1077 (77.7)	0.59
Number of AHT drugs prescribed	1.94 ± 0.93	1.98 ± 0.94	1.86 ± 0.91	< 0.001	2.01 ± 0.98	1.90 ± 0.90	0.043
AHT drugs							
Angiotensin inhibitor	1294 (61.0)	818 (61.9)	405 (60.5)	0.15	471 (62.3)	823 (60.2)	0.98
Calcium channel blocker	1219 (57.4)	744 (56.3)	390 (58.3)	0.81	445 (58.9)	774 (56.6)	0.07
Diuretic	1167 (55.0)	760 (57.5)	324 (48.4)	0.016	425 (56.2)	742 (54.3)	0.46
Beta-blocker	466 (22.0)	311 (23.5)	139 (20.8)	0.046	183 (24.2)	283 (20.7)	0.53
Centrally acting agents	79 (3.7)	43 (3.3)	34 (5.1)	0.27	32 (4.2)	47 (3.4)	0.08

Recent diagnosis of hypertension (< 1 year)	335 (15.6)	192 (14.4)	117 (17.1)	0.006	126 (16.5)	209 (15.0)	0.14
Systolic BP (mmHg)	149.1 ± 23.6	147.4 ± 22.7	152.1 ± 24.7	0.035	145.0 ± 21.5	151.3 ± 24.4	< 0.001
Diastolic BP (mmHg)	88.4 (14.3)	87.8 ± 13.6	89.4 ± 15.7	0.001	86.4 ± 12.4	89.5 ± 15.1	< 0.001
BMI (kg/m <sup>2</sup> )	27.9 ± 5.7	27.7 ± 5.6	28.3 ± 5.7	0.034	28.0 ± 5.7	27.8 ± 5.7	0.36
Cardiovascular risk factors							
None	461 (28.0)	297 (28.8)	133 (26.9)	0.37	162 (28.7)	299 (27.7)	0.74
Sedentary lifestyle	649 (39.5)	403 (39.0)	201 (40.6)	0.35	211 (37.4)	438 (40.5)	0.22
Hypercholesterolaemia	328 (19.9)	215 (20.8)	91 (18.4)	0.03	125 (22.2)	203 (18.8)	0.19
Diabetes mellitus	288 (17.5)	179 (17.3)	92 (18.6)	0.55	92 (16.3)	196 (18.1)	0.30
Hypertriglyceridaemia	88 (5.3)	50 (4.8)	31 (6.3)	0.30	30 (5.3)	58 (5.4)	0.31
Tobacco use	84 (5.1)	48 (4.6)	28 (5.7)	0.10	22 (3.9)	62 (5.7)	0.12
Adherence (poor versus good)							
Poor adherence to salt restriction	700 (34.0)	-	-	-	193 (26.0)	507 (38.4)	< 0.001
Poor adherence to medication	1416 (64.4)	812 (59.7)	507 (72.4)	< 0.001	-	-	-

Data are expressed as mean ± standard deviation or number (%). AHT: antihypertensive; BMI: body mass index; BP: blood pressure.

<sup>a</sup> *P* values were obtained by logistic regression analysis, adjusted for country.

**Table 2** Odds ratios for uncontrolled blood pressure level according to adherence to salt restriction or to medication

	% of patients with uncontrolled BP (95% CI)	OR <sup>a</sup> for uncontrolled BP (95% CI)	<i>P</i>
Adherence to salt restriction			
Good	75.7 (73.3–78.0)	1	
Poor	80.1 (77.0–83.0)	1.33 (1.03–1.72)	0.028
Adherence to medication			
Good	72.3 (69.0–75.4)	1	
Poor	80.3 (78.1–82.3)	1.56 (1.25–1.93)	< 0.001
Adherence to both salt restriction and medication			
Good	70.4 (66.4–74.2)	1	
Good adherence to medication and poor adherence to salt restriction	77.5 (70.9–83.2)	1.50 (0.99–2.28)	0.06
Poor adherence to medication and good adherence to salt restriction	79.3 (76.3–82.0)	1.62 (1.24–2.11)	< 0.001
Poor	81.2% (77.5–84.5)	1.91 (1.39–2.66)	< 0.001

BP: blood pressure; CI: confidence interval; OR: odds ratio.

<sup>a</sup>ORs were estimated by logistic regression, adjusted for age, sex and country, using good adherence as the reference category.

Figure 1

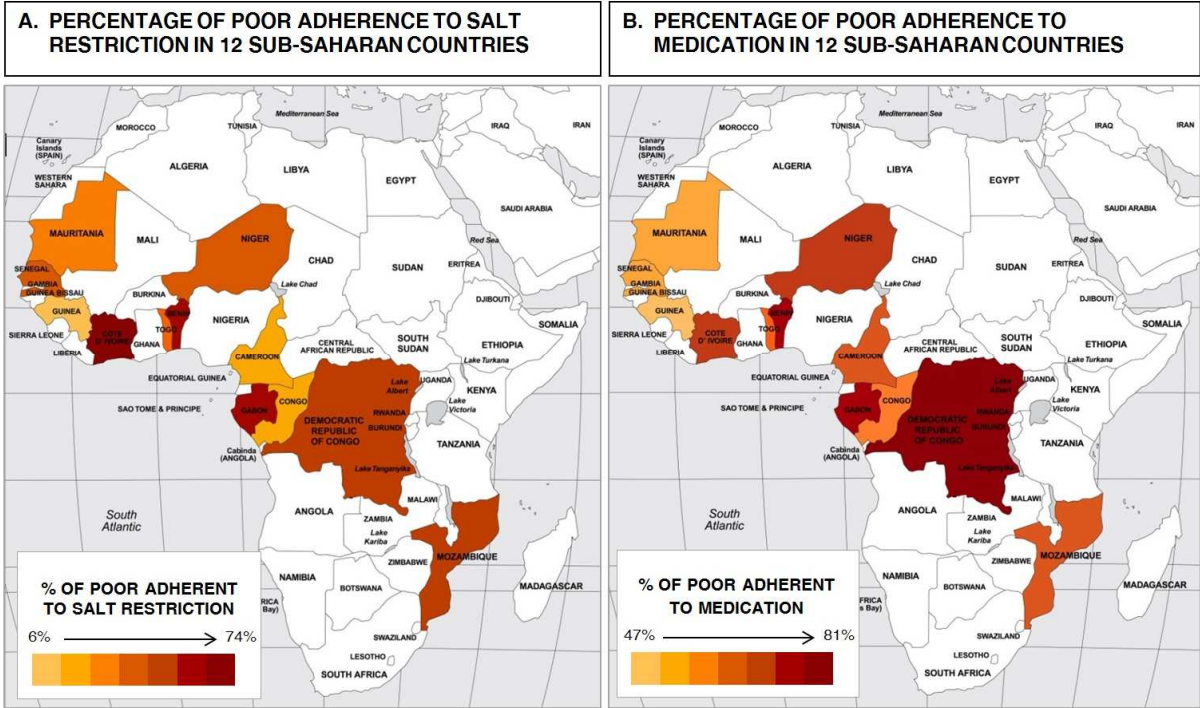




Figure 2

