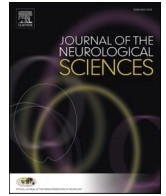




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Stroke occurrence by hypertension treatment status in Ghana and Nigeria: A case-control study

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ABSTRACT

Background: Hypertension is preeminent among the vascular risk factors for stroke occurrence. The wide gaps in awareness, detection, treatment, and control rates of hypertension are fueling an epidemic of stroke in sub-Saharan Africa.

Purpose: To quantify the contribution of untreated, treated but uncontrolled, and controlled hypertension to stroke occurrence in Ghana and Nigeria.

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Methods: The Stroke Investigative Research and Educational Network (SIREN) is a case-control study across 16 study sites in Ghana and Nigeria. Cases were acute stroke ($n = 3684$) with age- and sex-matched stroke-free controls ($n = 3684$). We evaluated the associations of untreated hypertension, treated but uncontrolled hypertension, and controlled hypertension at BP of $<140/90$ mmHg with risk of stroke occurrence. We assessed the adjusted odds ratio and population-attributable risk of hypertension treatment control status associated with stroke occurrence.

Results: The frequencies of no hypertension, untreated hypertension, treated but uncontrolled hypertension and controlled hypertension among stroke cases were 4.0%, 47.7%, 37.1%, and 9.2% vs 40.7%, 34.9%, 15.9%, and 7.7% respectively among stroke-free controls, $p < 0.0001$. The aOR and PAR (95% CI) for untreated hypertension were 6.58 (5.15–8.41) and 35.4% (33.4–37.4); treated but uncontrolled hypertension was 9.95 (7.60–13.02) and 35.9% (34.2–37.5); and controlled hypertension 5.37 (3.90–7.41) and 8.5% (7.6–9.5) respectively. Untreated hypertension contributed a PAR of 47.5% to the occurrence of intracerebral hemorrhage vs 29.5% for ischemic stroke. The aOR of untreated hypertension for stroke occurrence was 13.31 (7.64–23.19) for <50 years; 7.14 (4.51–11.31) for 50–64 years; and 3.48 (2.28–5.30) for 65 years or more.

Conclusion: The contribution of untreated hypertension and treated but uncontrolled hypertension to stroke occurrence among indigenous Africans is substantial. Implementing targeted interventions that address gaps in hypertension prevention and treatment, involving the local population, healthcare providers, and policymakers, can potentially substantially reduce the escalating burden of strokes in Africa.

1. Introduction

Hypertension is the preeminent modifiable risk factor for stroke globally [1]. The effect size of elevated blood pressure for stroke occurrence is most pronounced in low-income countries due to poor control of hypertension [2,3]. Sub-Saharan Africa (SSA) aptly exemplifies the global disparity in hypertension control where low levels of awareness, detection, and treatment are rife with only an estimated 7% of the 150 million adults with hypertension having their blood pressure under control [4–6]. An estimated 1 million deaths are attributed annually to hypertension in Africa alone [7]. Therefore, optimal blood pressure reduction lies at the centre of any serious effort to lessen the burden of stroke and indeed other cardiovascular diseases on the African continent. In pursuit of this goal, a clearer understanding of the contextual epidemiology of hypertension for stroke occurrence in SSA will have impactful ramifications for stroke prevention.

The population attributable risk (PAR) of hypertension for stroke occurrence among Ghanaians and Nigerians of 90.7% is staggering [8,9]. The PAR provides an estimate of the quantum of stroke that can be prevented by eliminating a risk factor such as hypertension. However, data on the extent to which untreated hypertension, treated but uncontrolled hypertension, and controlled hypertension differentially contribute to stroke occurrence in Africa are sparse. A better understanding of the contribution of hypertension treatment gaps to stroke occurrence will provide empirical evidence to inform policy directives to help curtail the menace of stroke. Furthermore, elucidating the extent to which gaps in hypertension control differ by key demographic indicators such as age and stroke types will broaden our understanding of stroke epidemiology in Africa. We sought to answer pertinent questions around stroke and hypertension within the Stroke Investigative Research and Educational Network (SIREN) study, which is currently the largest and most extensive epidemiological study of stroke in Africa.

2. Methods

2.1. Study design

The SIREN study is a multicenter case-control study involving 16 study sites in Ghana and Nigeria. There two tertiary medical centers in Ghana and 14 medical centers in Nigeria. A detailed protocol has been previously published [10]. We recruited consenting stroke cases who were ≥ 18 years old with first clinical stroke within 8 days of symptom onset or 'last seen without deficit'. In unconscious/aphasic patients, we sought consent from the next of kin. The clinical diagnoses of stroke and its types were confirmed by neuroimaging with a computerized tomography (CT) or magnetic resonance imaging (MRI) scan within ten

days of symptom onset. Stroke patients were recruited from hospitals to ensure rapid and accurate phenotyping.

2.2. Control subject recruitment

We recruited stroke-free adults, mainly from the communities in the catchment areas of the study sites, to serve as controls. Potential control subjects were screened using the 8-item questionnaire for verifying stroke-free status (QVSFS), which we previously validated [11]. Controls were matched to cases by age (± 5 years), sex and ethnicity to reduce the potential for confounding from these variables.

2.3. Standard Protocol Approvals, registrations, and patient consents

Ethical approval was obtained from all study sites, and informed consent was obtained from all participants [10].

3. Data collection

Demographic, socioeconomic, lifestyle (including cigarette smoking and alcohol use), physical activity, dietary intake, psychosocial stress, and depression information were obtained by self-report using validated instruments. Blood samples for HbA1c, and early morning samples after overnight fast in cases (post-acute phase when fasting is feasible) and controls for measurement of fasting lipid panel [total cholesterol (TC), high-density lipoprotein-cholesterol (HDL-C), low-density lipoprotein-cholesterol (LDL-C), and triglycerides (TG)] and fasting glucose were obtained following a uniform standard operating procedure across all study sites.

4. Definition of variables

- **Hypertension:** An average of three blood pressure (BP) measurements was obtained at baseline and daily for seven days or until death for stroke cases [2]. Hypertension was defined using a cutoff of $\geq 140/90$ mmHg at 72 h after stroke, a history of hypertension, or use of antihypertensive drugs before stroke or > 72 h after stroke. Many cases were either unaware of premorbid hypertensive status or were either aphasic or unconscious to provide information on the history of hypertension. Hence, the diagnosis of hypertension relied on BP measurements taken after an intracerebral hemorrhage (ICH), and to account for elevations in post-stroke BP in relation to premorbid BP, we made adjustments to systolic BP (SBP) by applying a correction factor of 0.8755 to SBPs of participants with intracerebral hemorrhage and 0.9358 to those with ischemic stroke in accordance with recommendations of the Oxford Vascular Study (OXVASC) [12].

- In control subjects, hypertension was defined as self-reported history of hypertension, use of antihypertensive drugs, or average BP at first clinical encounter $\geq 140/90$ mmHg [2]. Blood pressure measurements for control subjects were taken in the community.
- The definitions used for three strata of hypertension control were as follows:
 - **Untreated hypertension:** having an elevated blood pressure without a history of use of antihypertensive medications. This included those unaware of hypertension status and those aware but not receiving antihypertensive medication.
 - **Treated but uncontrolled hypertension:** A blood pressure of $>140/90$ mmHg with a reported history of current use of antihypertensive medications.
 - **Treated and controlled hypertension:** A blood pressure of $<140/90$ mmHg with a reported history of current use of antihypertensive medications.
- Diabetes mellitus (DM) was defined using either a history of diabetes mellitus, use of medications for DM, an elevated HBA1c $\geq 6.5\%$ or a fasting blood glucose (FBG) level ≥ 7.0 mmol/L for controls or FBG taken after seven days for stroke cases due to stress-induced transient rise in plasma glucose [13].
- Dyslipidemia was defined as either a fasting TC ≥ 5.2 mmol/L, LDL-C ≥ 3.4 mmol/L, HDL-C ≤ 1.03 mmol/L, or TG ≥ 1.7 mmol/L in accordance with the NCEP guidelines [14] or use of statin prior to stroke onset.
- Cardiac disease was defined on the basis of either history, clinical examination, and ECG or echocardiographic evidence of atrial fibrillation, heart failure, ischemic heart disease, cardiomyopathy, rheumatic heart disease, or valvular heart disease.
- Obesity: Subjects with waist-to-hip ratio (WHR) of 0.90 for men and 0.85 for women or a body mass index (BMI) ≥ 30 kg/m² were classified as obese using the World Health Organization cutoffs [15].
- Individuals were classified as physically active if they were regularly involved in moderate exercise (walking, or cycling) or strenuous exercise (jogging, football, and vigorous swimming) for 4 h or more per week [2].
- Dietary history: The regularity of consumption of food items such as green leafy vegetables, the addition of salt at the table, meat, fish, nuts, sugar and other local staple food items were classified on daily, weekly, at least once monthly and none in a month. Dose-response associations were assessed for green leafy vegetable consumption.
- Alcohol use was categorized into current users (users of any form of alcoholic drinks) or never/former drinker. We dichotomized alcohol intake as low (for males 1–3 drinks per day and 1–2 drinks per day for females) and high if consumption exceeded these sex-specific cutoffs [2].
- Smoking status was defined as current smoker (individuals who smoked any tobacco in the past 12 months) or former smoker (stopped for >12 months) or never smoked.
- Infarct or hematoma volumes were categorized into <10 cm³, 10–30 cm³, and >30 cm³.
- Stroke severity was assessed using the National Institutes of Health Stroke Scale.
- ECG evidence of left ventricular hypertrophy was defined using the Sokolow-Lyon voltage.
- Echocardiographic evidence of left ventricular (LV) hypertrophy was defined by the LV mass index calculated by dividing the value of LV mass by participant height to its allometric growth rate of 2.7 with a cut-off value of 51 g/height^{2.7}.
- Stroke fatality was defined as death during admission with an acute stroke.

5. Statistical analysis

We compared demographic, clinical and neuroradiological characteristics of stroke cases according to four hypertension categories (no

hypertension, untreated hypertension, treated but uncontrolled hypertension and treated and controlled hypertension). We compared continuous parametric variables using analysis of variance (ANOVA) and chi-squared test for categorical variables. We used conditional logistic regression models to determine the adjusted associations between stroke, its types and vascular risk factors. For hypertension, no hypertension was coded as the referent group for three hypertension categories of interest: untreated hypertension, treated but uncontrolled hypertension and treated and controlled hypertension. Sensitivity analyses assessing the associations of the three categories of hypertension control by stroke type (ischemic stroke and intracerebral hemorrhage), age (<50 years, 50–64 years, 65+ years) and by sex (male and female) were performed.

In addition, systolic blood pressure thresholds [<120 mmHg (as referent), 120–129 mmHg, 130–139 mmHg, 140–159 mmHg, 160–179 mmHg and ≥ 180 mmHg] and diastolic blood pressure thresholds [<80 mmHg (as referent), 80–89 mmHg, 90–99 mmHg, 100–109 mmHg, and ≥ 110 mmHg] were assessed for their associations with stroke occurrence and by stroke types. Furthermore, we assessed the association between stroke occurrence and number of pre-morbid antihypertensive drug classes specifying non-hypertensive group as the referent. Adjustments were made for potential confounders not used in the matching except baseline age which was included due to the non-exact age matching. In general, covariates were selected for inclusion in adjusted models after a literature review, our clinical understanding of stroke risk, and empirical evidence based on significant associations found in our initial bivariable analyses. The final adjusted models were assessed for collinearity using the goodness of fit via residual analysis and variance inflation factor (VIF) approaches. The odds ratio (OR) and 95% confidence intervals in our models were estimated using conditional likelihood. The adjusted population attributable risks (PARs) of hypertension categories of interest and stroke occurrence including its primary types were determined. We calculated the 95%CI for the PARs using the AF R-package [16] and estimated the variance using the delta method [17]. We estimated the PAR the three categories of hypertension control using the method described by Bruzzi [18]. Imputation for missing data was performed using multiple imputations by chain equations (MICE). All statistical tests of hypotheses were two-sided, with a p -value <0.05 considered significant. Statistical analyses and graphics were produced with SAS 9.4 and R statistical program (version 3.4.2).

6. Results

6.1. Demographic and risk factor profile of cases and controls

We enrolled 3684 stroke cases and 3684 age- and sex-matched stroke-free controls. The demographic and risk factor profile of stroke cases differed significantly from controls (Table S1). Among the stroke cases, there were 2573 (69.8%) with ischemic stroke and 1101 with intracerebral hemorrhage.

6.2. Hypertension control categories by stroke status and stroke types

The frequencies of no hypertension, untreated hypertension, treated but uncontrolled hypertension, and treated and controlled hypertension among stroke cases were 347 (4.0%), 1545 (47.7%), 1410 (37.1%) and 365 (9.2%). The corresponding frequencies among stroke free controls were 1498 (40.7%), 1285 (34.9%), 585 (15.9%), and 285 (7.7%) respectively, $p < 0.0001$. Table 1 also shows the frequency of hypertension control categories by stroke type namely ischemic stroke and ICH. Among 1545 stroke cases with untreated hypertension 546 (35.3%) were not aware of hypertension diagnosis while 999 (64.7%) were aware but not currently receiving antihypertensive medications. Correspondingly, among 1235 stroke free controls with untreated hypertension, 864 (70.0%) were not aware of hypertension diagnosis and 371(30.0%) were aware but not on treatment.

Table 1
Hypertension diagnosis, treatment, and control rates among stroke-free controls versus stroke cases by Stroke types.

	All stroke				Ischemic stroke				Intracerebral hemorrhage			
	Stroke free controls N = 3684	Stroke cases N = 3684	P-value	Unadjusted odds ratio (95% CI)	Stroke free controls N = 2573	Ischemic Stroke cases N = 2573	P-value	Unadjusted odds ratio (95% CI)	Stroke free controls N = 1101	ICH cases N = 1101	P-value	Unadjusted odds ratio (95% CI)
No hypertension	1498 (40.7)	148 (4.0)	<0.0001	1	1002 (38.9)	128 (5.0)	<0.0001	1	492 (44.7)	19 (1.7)	<0.0001	1
Untreated hypertension	1285 (34.9)	1759 (47.7)		16.41 (12.87, 20.92)	911 (35.4)	1123 (43.6)		11.38 (8.77, 14.76)	368 (33.4)	633 (57.5)		72.60 (32.33, 163.07)
Treated but uncontrolled hypertension	585 (15.9)	1366 (37.1)		29.93 (23.11, 38.74)	417 (16.2)	978 (38.0)		21.95 (16.63, 28.96)	168 (15.3)	387 (35.1)		117.04 (50.99, 268.60)
Treated and controlled hypertension	285 (7.7)	338 (9.2)		15.38 (11.49, 20.61)	224 (8.7)	290 (11.3)		12.57 (9.20, 17.18)	61 (5.5)	46 (4.2)		35.35 (14.14, 88.35)

6.3. Demographic and clinical features of stroke cases by hypertension control categories

The mean age of stroke cases increased significantly across the hypertension control categories, being lowest at 54.9 years for those without hypertension and 64.0 years for those with treated and controlled hypertension, $p < 0.0001$. Similarly, the proportions with dyslipidemia, diabetes, and cardiac disease were lowest among those without hypertension and highest among those with treated and controlled hypertension (Table 2). Significant differences in dietary practices were observed across the three groups with hypertension. For example, low vegetable consumption, addition of salt at table, regular sugar consumption was least frequently observed among those with treated and controlled hypertension group compared with those with untreated hypertension and treated but uncontrolled hypertension.

The frequency of intracerebral hemorrhage was highest at 36.8% among those with untreated hypertension and lowest among those with treated and controlled hypertension at 14.8%. Proportion with a volume of small stroke lesions $<10 \text{ cm}^3$ was lowest among those without hypertension. (Table 2). Stroke case fatality was 15% among those without hypertension, 22.7% among untreated hypertension, 18.8% among treated but uncontrolled hypertension, and 18.9% among treated and controlled hypertension group, $p = 0.039$.

6.4. Associations between hypertension control categories and stroke occurrence

The overall adjusted odds ratio (aOR) and adjusted population attributable risk (PAR) (95%CI) of hypertension for stroke occurrence was 7.29 (5.76–9.20) and 79.4% (76.1–82.7%). The aOR and PAR of hypertension for ischemic stroke was 5.54 (4.20–7.31) and 74.6% (69.6–79.6%) respectively and 13.85 (8.62–22.25) and 87.5% (83.6–91.4%) for ICH. The partitioned aOR and PAR by hypertension control categories with no hypertension as referent were 6.58 and 35.37% for untreated hypertension, 9.95 and 35.85% for treated but uncontrolled hypertension, and 5.37 and 8.53% for treated and controlled hypertension (Table 3). By stroke types, the PAR of untreated hypertension for ischemic stroke was lower at 29.47% compared with 47.47% for ICH, while that for controlled hypertension was 10.36% for ischemic stroke versus 4.00% for ICH (Figs. 1–3). There were no significant differences in the effect sizes of hypertension strata by sex (Table S2). However, by age, we observed significant differences in the magnitude and direction of hypertension treatment status and stroke occurrence with those <50 years with higher adjusted OR for untreated hypertension for stroke occurrence 13.31 (7.64–23.19), followed by those 50–64 years, 7.14 (4.51–11.31) and finally those 65 years or more 3.48 (2.28–5.30) (Table S3).

6.5. Stroke risk by admission blood pressure levels and reported pre-morbid antihypertensive medication use

The adjusted OR of admission systolic and diastolic blood pressure levels with stroke occurrence relative to stroke-free controls are shown in Table 4 and Fig. 4. The association between admission systolic and diastolic blood pressure showed a gradual/steady rise with risk of ischemic stroke occurrence, but that for ICH depicted a rather steep ascent with rising BP levels. Regarding the effect of pre-morbid antihypertensive use on stroke occurrence, the PAR of stroke occurrence is lowest with 3 or more antihypertensives, particularly for ICH (Table 5).

7. Discussion

Hypertension is pervasive among indigenous Africans with stroke. Our present analysis highlights the contribution of the enormous treatment gaps in hypertension to stroke occurrence. Up to 96% of stroke cases had hypertension, partitioned into 48% with untreated hypertension, 37% with uncontrolled hypertension on treatment, and only 9% had controlled hypertension at presentation with stroke. Consequently, the adjusted population attributable risk of hypertension for stroke occurrence overall was 79%, divided into 8.5% for controlled hypertension, 35.9% for uncontrolled hypertension on antihypertensives, and 35.4% for untreated hypertension. Among age- and sex-matched stroke free controls up to 60% had hypertension, attesting to the significant burden of elevated blood pressure and its impact in the sub-Saharan African adult population [6].

Untreated hypertension contributed more to the occurrence of intracerebral hemorrhage, a highly fatal stroke type, with a PAR of 47%. In the present analysis, untreated hypertension comprised those unaware of their hypertension status and those aware but not receiving antihypertensive medications. Close to one-third of stroke cases with untreated hypertension were unaware of hypertension diagnosis, with the remaining two-thirds not on antihypertensive medications despite being aware of hypertension diagnosis. However, for stroke-free controls with up to 70% of those with untreated hypertension were unaware of their diagnosis. Notably, those with untreated hypertension before stroke onset were demographically the youngest by age. We found that untreated hypertension prior to stroke onset was associated with the highest stroke severity scores and stroke fatality rates of 22.7%, primarily driven by the higher preponderance of ICH [19,20].

Up to 37% of stroke cases and 16% of stroke-free controls reported being on antihypertensive medications but had uncontrolled blood pressure. Poorly controlled hypertension was associated with a higher adjusted odds ratio of 20.7 for intracerebral hemorrhage compared with 7.4 for ischemic stroke. An admixture of patient-level factors such as medication non-adherence, provider-level factors, notably clinician

Table 2
Comparison of demographic, lifestyle, vascular risk profile and clinical features of stroke cases by hypertension status.

Variable	No hypertension <i>n</i> = 347	Untreated hypertension <i>n</i> = 1545	Treated but uncontrolled hypertension <i>n</i> = 1410	Treated and controlled hypertension <i>n</i> = 365	P-value
Country, Ghana, n (%)	120 (34.6)	474 (30.7)	410 (29.1)	166 (45.5)	<0.0001
Male sex, n (%)	184 (53)	894 (57.9)	730 (51.8)	176 (48.2)	0.001
Age, mean ± SD	54.9 ± 18.4	57.7 ± 13.8	61.31 ± 12.6	64.0 ± 12.6	<0.0001
Domicile					
<i>Rural</i> , n (%)	37 (10.7)	148 (9.6)	107 (7.6)	36 (9.9)	0.010
<i>Semi-urban</i> , n (%)	118 (34)	471 (30.5)	391 (27.7)	109 (29.9)	
<i>Urban</i> , n (%)	181 (52.2)	920 (59.5)	906 (64.3)	219 (60)	
Monthly Income >\$100, n (%)	165 (47.6)	844 (54.6)	754 (53.5)	202 (55.3)	0.352
Education, (some) n (%)	268 (77.2)	1262 (81.7)	1139 (80.8)	271 (74.2)	0.012
Vascular risk factors					
Systolic blood pressure, mean (SD)	119.5 (12.2)	163.8 (30.2)	170.4 (24.8)	123.6 (11.2)	<0.0001
Diastolic blood pressure, mean (SD)	74.2 (8.6)	98.8 (17.8)	101.2 (15.8)	75.9 (7.9)	<0.0001
Number of antihypertensive meds pre-stroke, mean (SD)	0.0 (0.0)	0.0 (0.0)	1.4 (0.8)	1.5 (0.9)	<0.0001
Number of antihypertensives, n (%)					
0	347 (100)	1545 (100)	123 (8.7)	36 (9.9)	<0.0001
1	0 (0.0)	0 (0.0)	653 (46.3)	159 (43.6)	
2	0 (0.0)	0 (0.0)	469 (33.3)	118 (32.3)	
3+	0 (0.0)	0 (0.0)	165 (11.7)	52 (14.2)	
Duration of hypertension, years	0 (0.0)	6.2 (7.8)	7.7 (8.1)	12.3 (14.9)	<0.001
Pre-admission antihypertensives with Known hypertension, n (%)					
ACE-Inhibitors	0 (0)	0 (0)	425 (30.1)	115 (31.5)	<0.000
Angiotensin receptor blockers	0 (0)	0 (0)	91 (6.5)	35 (9.6)	
Beta-blockers	0 (0)	0 (0)	76 (5.4)	32 (8.8)	<0.0001
Calcium channel blockers	0 (0)	0 (0)	691 (49)	175 (47.9)	<0.0001
Diuretic	0 (0)	0 (0)	534 (37.9)	132 (36.2)	<0.0001
Alpha blockers	0 (0)	0 (0)	24 (1.7)	6 (1.6)	<0.0001
Methyl dopa	0 (0)	0 (0)	135 (9.6)	30 (8.2)	<0.0001
Dyslipidemia, n (%)	188 (54.2)	1010 (65.4)	1025 (72.7)	259 (71)	<0.0001
Diabetes	66 (19)	484 (31.3)	638 (45.2)	178 (48.8)	
Cardiac Disease, n (%)	33 (9.5)	118 (7.6)	185 (13.1)	59 (16.2)	<0.0001
Atrial fibrillation, n (%)	9 (2.6)	44 (2.8)	78 (5.5)	27 (7.4)	<0.0001
HDL-Cholesterol, mg/dl, mean ± SD	46.8 ± 20.9	48.5 ± 19.9	48.1 ± 19.0	45.5 ± 18.5	0.088
LDL-Cholesterol, mg/dl, mean ± SD	116.1 ± 53.7	121.4 ± 50.3	123.6 ± 52.6	114.9 ± 49.5	0.021
LDL/HDL ratio, mean ± SD	2.8 ± 1.7	2.9 ± 2.0	2.9 ± 1.7	3.0 ± 1.9	0.885
Total Cholesterol, mmol/l, mean ± SD	183.9 ± 59.1	193.1 ± 55.9	193.6 ± 59.1	183.9 ± 56.1	0.006
Triglyceride, mg/dl, mean ± SD	127.0 ± 82.9	120.3 ± 75.3	135.2 ± 92.5	125.2 ± 80.7	<0.0001
76.3 (45.0,					
Serum creatinine, median (IQR)	102.0)	71.0 (1.4, 103.0)	74.0 (1.7, 108.5)	81.0 (51.3, 113.0)	0.001
Waist-to-hip Ratio, mean ± SD	0.92 ± 0.1	0.94 ± 0.1	0.95 ± 0.1	0.94 ± 0.1	0.002
Waist-to-hip Ratio raised, n (%)	82 (23.6)	521 (33.7)	532 (37.7)	120(32.9)	0.006
BMI*** (kg/m ²), mean ± SD	25.3 ± 4.9	26.4 ± 5.1	27.3 ± 5.3	26.9 ± 5.3	<0.001
BMI*** > 30 kg/m ² , n (%)	40 (11.5)	242 (15.7)	264 (18.7)	71 (19.5)	0.001
Physical inactivity	12 (3.5)	37 (2.4)	98 (7.0)	24 (6.6)	<0.0001
Tobacco (any use), n (%)	28 (8.1)	150 (9.7)	115 (8.2)	29 (7.9)	0.399
Alcohol (current user), n (%)	40 (11.5)	295 (19.1)	180 (12.8)	56 (15.3)	<0.0001
Stress, n (%)	53 (15.3)	248 (16.1)	272 (19.3)	82 (22.5)	0.036
Cancer, n (%)	2 (0.6)	2 (0.1)	8 (0.6)	12 (3.3)	<0.0001
Depression, n (%)	18 (5.2)	104 (6.7)	102 (7.2)	35 (9.6)	0.488
Family history of CVD, n (%)	77 (22.2)	515 (33.3)	580 (41.1)	164 (44.9)	<0.0001
Family history hypertension	57 (16.4)	462 (29.9)	539 (38.2)	141 (38.6)	<0.0001
Adding salt at table, n (%)	24 (6.9)	125 (8.1)	80 (5.7)	10 (2.7)	<0.0001
Adding salt at table categories:					
<i>Never/rarely</i> , n (%)	255 (73.5)	1346 (87.1)	1289 (91.4)	345 (94.5)	<0.0001
<i>Occasionally</i> , n (%)	255 (73.5)	1346 (87.1)	1289 (91.4)	345 (94.5)	<0.0001
<i>Very often</i> , n (%)	24 (6.9)	125 (8.1)	80 (5.7)	10 (2.7)	
Low vegetable consumption, n (%)	74 (21.3)	458 (29.6)	311 (22.1)	79 (21.6)	<0.0001
Whole grains consumption, n (%)	199 (57.3)	1179 (76.3)	1152 (81.7)	291 (79.7)	<0.0001
Legumes consumption, n (%)	170 (49)	899 (58.2)	908 (64.4)	226 (61.9)	0.246
Fruit consumption, n (%)	214 (61.7)	1174 (76)	1155 (81.9)	290 (79.5)	0.037
Sugar consumption or otherwise, n (%)	69 (19.9)	449 (29.1)	347 (24.6)	83 (22.7)	<0.0001
Meat consumption or otherwise, n (%)	190 (54.8)	1061 (68.7)	1022 (72.5)	232 (63.6)	0.003
Fish consumption or otherwise, %	233 (67.1)	1283 (83)	1244 (88.2)	313 (85.8)	0.018

Neuro-radiological correlates

Stroke type

(continued on next page)

Table 2 (continued)

Variable	No hypertension <i>n</i> = 347	Untreated hypertension <i>n</i> = 1545	Treated but uncontrolled hypertension <i>n</i> = 1410	Treated and controlled hypertension <i>n</i> = 365	P-value
<i>Ischemic</i>	265 (76.4)	973 (63)	1011 (71.7)	309 (84.7)	<0.0001
<i>Intracerebral hemorrhage</i>	78 (22.5)	569 (36.8)	398 (28.2)	54 (14.8)	
Volume of lesion (cm ³)					0.009
<10	174 (50.1)	886 (57.3)	832 (59)	221 (60.5)	
10–30	61 (17.6)	347 (22.5)	230 (16.3)	63 (17.3)	
>30	5 (1.4)	29 (1.9)	17 (1.2)	3 (0.8)	
Location of lesion					
Hemorrhagic strokes					0.323
<i>Lobar</i>	20 (5.8)	107 (6.9)	84 (6.0)	12 (3.3)	
<i>Non-lobar</i>	48 (13.8)	426 (27.6)	287 (20.4)	39 (10.7)	
Stroke etiology					
Ischemic stroke					
TOAST classification					
<i>Large vessel atherosclerosis</i>	71 (20.5)	302 (19.5)	261 (18.5)	78 (21.4)	0.071
<i>Small-vessel occlusion or lacunar</i>	65 (18.7)	280 (18.1)	307 (21.8)	89 (24.4)	
<i>Cardio-embolic</i>	16 (4.6)	58 (3.8)	48 (3.4)	31 (8.5)	
<i>Others</i>	61 (17.6)	248 (16.1)	241 (17.1)	69 (18.9)	
Hemorrhagic Stroke					
SMASH-U Etiologic classes					
<i>Structural</i>	11 (3.2)	13 (0.8)	11 (0.8)	3 (0.8)	<0.0001
<i>Medication-associated</i>	1 (0.3)	1 (0.1)	2 (0.1)	0 (0)	
<i>Amyloid Angiopathy</i>	1 (0.3)	3 (0.2)	5 (0.4)	2 (0.5)	
<i>Systemic diseases</i>	1 (0.3)	1 (0.1)	2 (0.1)	0 (0)	
<i>Hypertension</i>	42 (12.1)	426 (27.6)	279 (19.8)	39 (10.7)	
<i>Undetermined</i>	3 (0.9)	10 (0.6)	8 (0.6)	1 (0.3)	
Stroke severity indicators					
NIHSS score, mean ± SD	13.3 ± 11.2	15.6 ± 11.7	14.9 ± 11.2	13.5 ± 10.6	0.002
Modified Rankin score	3.7 ± 1.3	3.8 ± 1.2	3.8 ± 1.1	3.7 ± 1.2	0.012
Subclinical vascular markers					
Left ventricular hypertrophy (ECG)	66 (19)	496 (32.1)	504 (35.7)	93 (25.5)	<0.0001
Left ventricular hypertrophy (Echo)	37 (10.7)	209 (13.5)	250 (17.7)	50 (13.7)	0.071
Carotid Intimal Media thickness, mean ± SD	1.7 ± 0.5	1.9 ± 0.6	2.0 ± 1.5	1.8 ± 0.5	0.078
Carotid Intimal Media thickness > 1 mm, n (%)	94 (27.1)	435 (28.2)	407 (28.9)	111 (30.4)	0.044
Carotid plaques, n (%)	8 (2.3)	49 (3.2)	52 (3.7)	14 (3.8)	0.497
Periventricular white matter disease					
<i>Mild</i>	65 (18.7)	267 (17.3)	315 (22.3)	82 (22.5)	0.164
<i>Moderate</i>	37 (10.7)	219 (14.2)	222 (15.7)	81 (22.2)	
<i>Severe</i>	6 (1.7)	46 (3)	45 (3.2)	9 (2.5)	
STROKE FATALITY, n (%)	52 (15)	350 (22.7)	265 (18.8)	69 (18.9)	0.039

inertia in a timely intensification of antihypertensive medications [21], and system-level factors, including medication stockouts, to name a few, collectively contribute to a substantial burden of uncontrolled hypertension on therapy in SSA. Previous studies from Africa have reported abysmally low blood pressure control rates under therapy among hypertensive patients across hospitals and clinics [4–6]. Our study estimates that the adjusted PAR of treated but poorly controlled hypertension for stroke occurrence is quite substantial at 36%. The PAR associated with antihypertensive medication was lowest among those on three or more antihypertensives. The European Society of Cardiology has recommended an initial two-drug therapy for most hypertensives given the multifactorial genesis of hypertension and the need to moderate hypertension-mediated organ damage [21].

Treated and controlled hypertension retained a residual risk with stroke occurrence with 5.37 higher odds of stroke. The import of the significant and lingering risk for stroke occurrence despite being controlled on antihypertensive therapy is intriguing. Evidence from prospective cohort studies has clearly demonstrated that successful pharmacological treatment of hypertension attenuates but does not eliminate, the deleterious effects of hypertension on stroke risk [22,23]. For instance, a US study showed that successfully treated systolic BP target <140 mmHg had between 1.42 and 2.48 times greater risk of a stroke compared with normotensive individuals not on treatment [22].

Plausible explanations for the association between treatment-controlled hypertension and stroke occurrence include the observation that blood pressure control status is not a permanent state and is subject to surges which may predispose to the occurrence of stroke. Secondly, in our study we found that those with treatment-controlled hypertension frequently had carotid intimal media thickness > 1 mm suggesting a predisposition to vascular damage from vascular ageing and atherosclerosis. Thirdly, those with treatment-controlled hypertension had the highest effect sizes for other vascular risk factors including dyslipidemia, diabetes, and cigarette smoking compared with other hypertensive categories suggesting the need to optimize overall cardiovascular risk reduction in this sub-population with controlled hypertension. Fourth, it is best to prevent hypertension occurrence through early lifestyle interventions.

7.1. Implications

Our observations converge on a theme that untreated and poorly controlled hypertension exerts a more significant toll on a younger demographic population, among whom the devastating effects of stroke could potentially be mitigated through improved health promotion via hypertension screening and detection, with linkage to care for blood pressure control. O'Donnell and colleagues have used the INTERSTROKE database to demonstrate that the effect size of undiagnosed and

Table 3
Associations between Vascular risk factors including hypertension control categories and stroke occurrence.

	All stroke		Ischemic stroke		Intracerebral hemorrhage	
	Adjusted OR (95% CI)	PAR	Adjusted OR (95% CI)	PAR	Adjusted OR (95% CI)	PAR
No hypertension	1.00		1.00		1.00	
Untreated hypertension	6.58 (5.15, 8.41)	35.37 (33.37, 37.37)	4.71 (3.51, 6.30)	29.47 (26.67, 32.25)	14.70 (8.90, 24.29)	47.47 (44.68, 50.25)
Treated but uncontrolled hypertension	9.95 (7.60, 13.02)	35.85 (34.24, 37.46)	7.44 (0.43, 10.19)	35.18 (32.85, 37.50)	20.65 (11.86, 35.95)	36.31 (34.11, 38.51)
Treated and controlled hypertension	5.37 (3.90, 7.41)	8.53 (75.60, 9.50)	5.01 (3.45, 7.26)	10.36 (8.98, 11.73)	4.38 (2.21, 8.67)	4.00 (2.74, 5.26)
Dyslipidemia	1.43 (1.21, 1.68)	21.27 (12.85, 29.69)	1.33 (1.09, 1.64)	17.87 (6.98, 28.76)	1.84 (1.36, 2.50)	32.36 (19.81, 44.92)
Diabetes mellitus	3.32 (2.72, 4.05)	25.49 (22.88, 28.09)	3.73 (2.94, 4.72)	29.42 (26.37, 32.48)	2.79 (1.88, 4.13)	18.26 (13.33, 23.20)
Meat consumption	1.63 (1.36, 1.95)	28.58 (20.12, 37.02)	1.53 (1.23, 1.89)	25.41 (14.64, 36.17)	2.15 (1.53, 3.02)	39.76 (26.97, 52.55)
Low vegetable consumption	2.13 (1.75, 2.59)	15.30 (12.52, 18.08)	2.24 (1.76, 2.84)	15.18 (12.06, 18.32)	1.92 (1.34, 2.75)	15.26 (9.17, 21.34)
Obesity	1.55 (1.30, 1.85)	27.25 (18.77, 35.73)	1.65 (1.33, 2.04)	30.59 (20.48, 40.69)	1.40 (1.00, 1.94)	20.94 (5.00, 36.88)
Cardiac disease	1.59 (1.18, 2.14)	3.75 (1.65, 5.84)	2.04 (1.44, 2.91)	6.20 (3.79, 8.62)	0.69 (0.37, 1.28)	-2.54 (-7.60, 2.50)
Cigarette smoking (current)	3.32 (1.87, 5.91)	2.33 (1.65, 3.02)	2.88 (1.38, 5.99)	1.70 (0.88, 2.52)	4.36 (1.59, 11.95)	3.79 (2.58, 5.00)
Stress	1.59 (1.29, 1.96)	7.81 (4.87, 10.75)	1.61 (1.25, 2.08)	8.06 (4.48, 11.63)	1.36 (1.59, 11.95)	4.84 (-1.51, 11.20)
Physical inactivity	1.88 (1.19, 2.97)	1.88 (0.77, 2.99)	2.00 (1.14, 3.48)	2.07 (0.75, 3.40)	2.02 (0.86, 4.77)	1.89 (-0.00, 0.04)
Table added salt (Often)	1.47 (1.07, 2.01)	2.43 (0.79, 4.08)	1.25 (0.85, 1.84)	1.40 (-0.73, 3.53)	2.33 (1.29, 4.20)	8.23 (2.91, 7.55)
TOTAL PAR		78.75 (2.54, 84.95)		75.58 (67.44, 83.72)		84.49 (76.11, 92.86)

Additional adjustment for age (≥ 50), educational attainment (Some), location of residence(urban/semi-urban), monthly income (socio-demographic covariates).

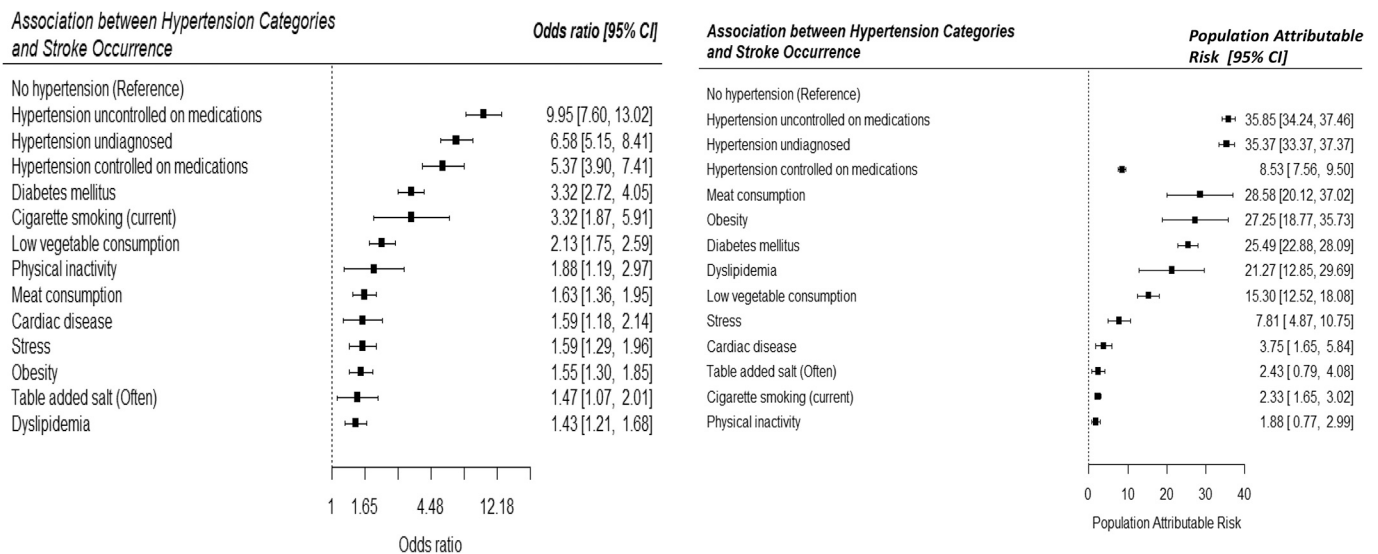


Fig. 1. All Stroke.

untreated hypertension correlates with gross national income across the globe [3]. They showed that low-income countries which harboured the highest burden of uncontrolled hypertension therefore had a preponderance of ICH which disproportionately affected a much younger population < 50 years old, as corroborated in our study.

In response to the growing threat posed by hypertension, we have recently proposed the African Control of Hypertension through Innovative Epidemiology and a Vibrant Ecosystem (ACHIEVE) to implement the HEARTS package for improved hypertension control in SSA [24]. We seek to develop and deploy pragmatic and contextualized interventions made up of 10 key strategic actions for addressing and surmounting the myriad of barriers to hypertension control in Africa. Our goal is to achieve 80% diagnosis of hypertension, 80% of hypertensives on

treatment and 80% of all hypertensives controlled by 2030. For health promotion purposes linking the occurrence of stroke, as a prototypical CVD, with hypertension will motivate the general public towards hypertension screening, detection and treatment. A team-based approach to hypertension care in the health delivery system across countries with task sharing to non-physicians and implementation of hypertension guidelines will bolster blood pressure and vascular risk control in constrained healthcare settings. Finally, by providing estimates on PAR of hypertension for stroke by the three strata of untreated, uncontrolled on treatment, and controlled, we hope to inspire and stimulate active participation by advocacy groups, policymakers, and health ministers to the menace of hypertension for redress. Primary prevention of stroke using mobile health interventions [27] along with task shifting for

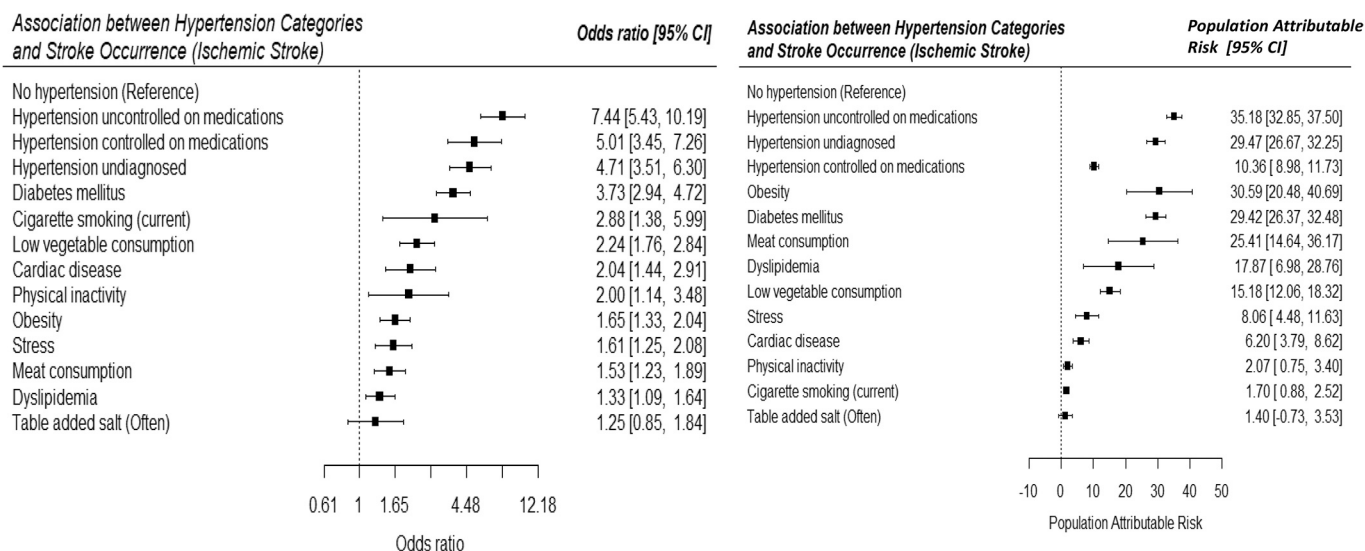


Fig. 2. Ischemic Stroke.

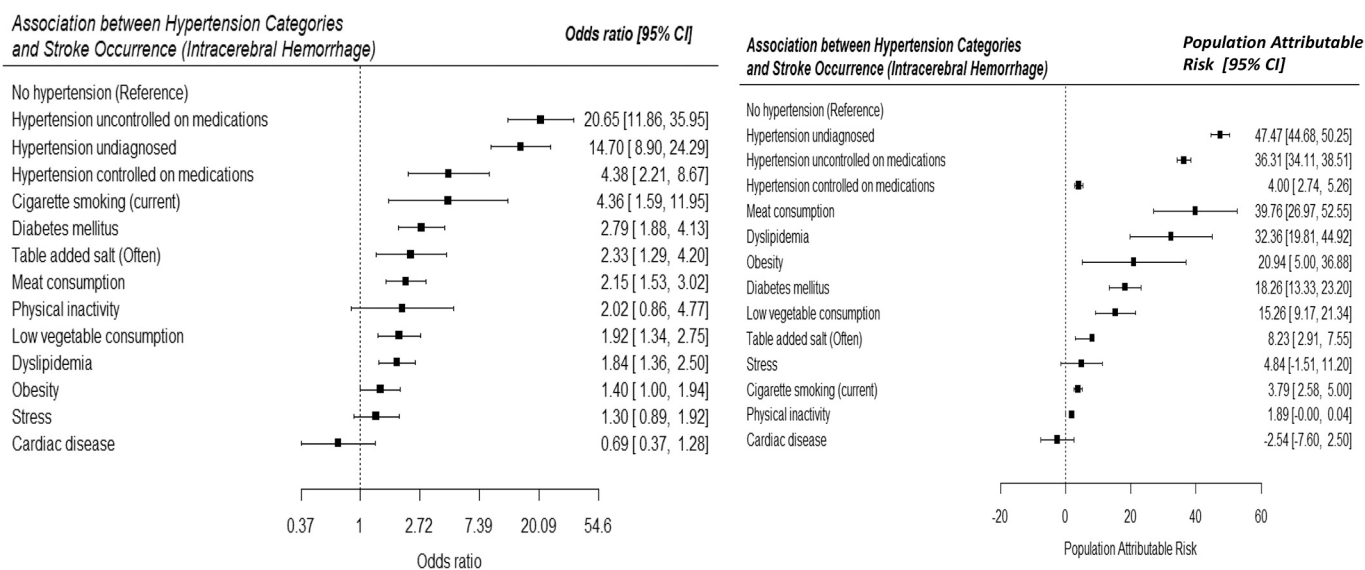


Fig. 3. Intracerebral hemorrhage.

treatment of hypertension [28] have shown promising preliminary results and can help mitigate stroke occurrence and in turn assuage the poor outcomes of stroke in the region [29,30].

7.2. Strengths and limitations

The reported effect sizes derived from this case-control study estimates associations rather than causation between hypertension and stroke occurrence. The blood pressure values obtained after admission with stroke may not reflect pre-morbid values before stroke onset. Being mindful of post-stroke elevation in blood pressure, we applied a correction factor proposed by Fischer to obtain approximate pre-morbid blood pressure values in our current analysis. Also, we did not assess medication adherence and dosages of antihypertensive medications prescribed. This information would have helped assess the contribution of resistant hypertension [25,26], shown to be rife among indigenous Africans. Despite these shortcomings, this is the most extensive study from Africa to report on the attributable fractions of hypertension status and treatment control categories to the occurrence of stroke and by its types.

8. Conclusions

The impact of untreated hypertension and poorly controlled hypertension on the occurrence of strokes among indigenous Africans is enormous. Enhancing surveillance, prevention, and treatment of hypertension through tailored interventions involving the population, healthcare providers, and policymakers as key stakeholders will substantially mitigate the contribution of hypertension to stroke occurrence throughout Africa.

Author contribution

MO and BO designed the study; FSS wrote the first draft of the manuscript, OAM and JOA performed data analyses, MO, and OAM have accessed and verified the data, all other co-authors reviewed the manuscript and agree to its submission.

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Table 4
Effect size of systolic and diastolic blood pressure levels among stroke-free controls versus stroke cases by Stroke types.

Systolic BP	All stroke					Ischemic stroke					Intracerebral hemorrhage				
	Stroke free controls N = 3684	Stroke cases N = 3684	P-value	Unadjusted odds ratio (95% CI)	Adjusted odds ratio (95% CI)	Stroke free controls N = 2573	Ischemic Stroke cases N = 2573	P-value	Unadjusted odds ratio (95% CI)	Adjusted odds ratio (95% CI)	Stroke free controls N = 1101	ICH cases N = 1101	P-value	Unadjusted odds ratio (95% CI)	Adjusted odds ratio (95% CI)
<120 mmHg	735 (20.0)	295 (8.0)	<0.0001	1	1	949 (36.9)	474 (18.4)	<0.0001	1	1	632 (57.4)	189 (17.2)	<0.0001	1	1
120–129 mmHg	735 (20.0)	298 (8.1)		1.02 (0.83, 1.26)	1.23 (0.93, 1.64)	432 (16.8)	328 (12.7)		1.71 (1.41, 2.09)	1.70 (1.28, 2.67)	174 (15.8)	97 (8.8)		1.81 (1.28, 2.58)	1.74 (1.11, 2.73)
130–139 mmHg	613 (16.6)	423 (11.5)		1.80 (1.47, 2.20)	1.91 (1.45, 2.50)	367 (14.3)	325 (12.6)		1.87 (1.54, 2.29)	1.47 (1.11, 1.96)	93 (8.4)	124 (11.3)		3.90 (2.70, 5.62)	4.37 (2.68, 7.12)
140–159 mmHg	837 (22.7)	853 (23.2)		2.60 (2.17, 3.13)	2.46 (1.92, 3.17)	519 (20.2)	731 (28.4)		3.03 (2.55, 3.62)	2.37 (1.85, 3.03)	143 (13.0)	311 (28.2)		6.33 (4.65, 0.62)	6.27 (4.13, 9.52)
160–179 mmHg	439 (11.9)	759 (20.6)		4.50 (3.69, 5.50)	4.18 (3.18, 5.50)	166 (6.5)	368 (14.3)		5.20 (4.08, 6.61)	5.10 (3.62, 7.21)	30 (2.7)	219 (19.9)		20.21 (12.54, 2.55)	22.53 (12.07, 42.06)
≥ 180 mmHg	231 (6.3)	967 (26.3)		10.54 (8.46, 13.14)	11.36 (8.44, 15.28)	64 (2.5)	279 (10.8)		8.87(6.51, 12.09)	7.92 (5.13, 12.23)	11 (1.0)	144 (13.1)		40.68 (19.51, 84.78)	41.26 (17.89, 95.20)
Diastolic BP															
<80 mmHg	1438 (39.0)	596 (16.2)	<0.0001	1	1	996 (38.7)	484 (18.8)	<0.0001	1	1	440 (40.0)	112 (10.2)	<0.0001	1	1
80–89 mmHg	979 (26.6)	696 (18.9)		1.71 (1.48, 1.98)	1.82 (1.49, 2.23)	677 (26.3)	558 (21.7)		1.68 (1.43, 1.98)	1.78 (1.41, 2.25)	298 (27.1)	136 (12.4)		1.78(1.28, 2.48)	2.10 (1.36, 3.26)
90–99 mmHg	684 (18.6)	755 (20.5)		2.79 (2.38, 3.26)	2.69 (2.16, 3.35)	473 (18.4)	563 (21.9)		2.58 (2.16, 3.07)	2.24 (1.73, 2.89)	208 (18.9)	190 (17.3)		3.61 (2.57, 35.08)	4.55 (2.87, 7.21)
100–109 mmHg	295 (8.0)	730 (19.8)		6.28 (5.21, 7.58)	5.93 (4.61, 7.62)	218 (8.5)	484 (18.8)		4.85 (3.93, 6.00)	4.25 (3.17, 5.71)	76 (6.9)	245 (22.3)		12.58 (8.37, 19.91)	14.71 (8.59, 25.19)
≥ 110 mmHg	193 (5.2)	817 (22.2)		10.25 (8.34, 12.60)	10.38 (7.83, 13.75)	133 (5.2)	416 (16.2)		6.58 (5.15, 8.39)	6.00 (4.22, 8.41)	60 (5.4)	400 (36.3)		24.71 (16.20, 37.71)	29.95 (17.21, 52.14)

Adjustment for Dyslipidemia, diabetes mellitus, meat consumption, low vegetable consumption, obesity, cardiac disease, cigarette smoking, stress, physical inactivity, table-added salt, age /(>=50), sex, educational attainment (Some), location of residence(urban/semi-urban), monthly income (socio-demographic covariates).

Note: For those with ischemic stroke, an adjustment factor of 0.9358 to systolic blood pressure was applied; for those with intracerebral hemorrhage, an adjustment factor of 0.8755 to systolic blood pressure was applied.

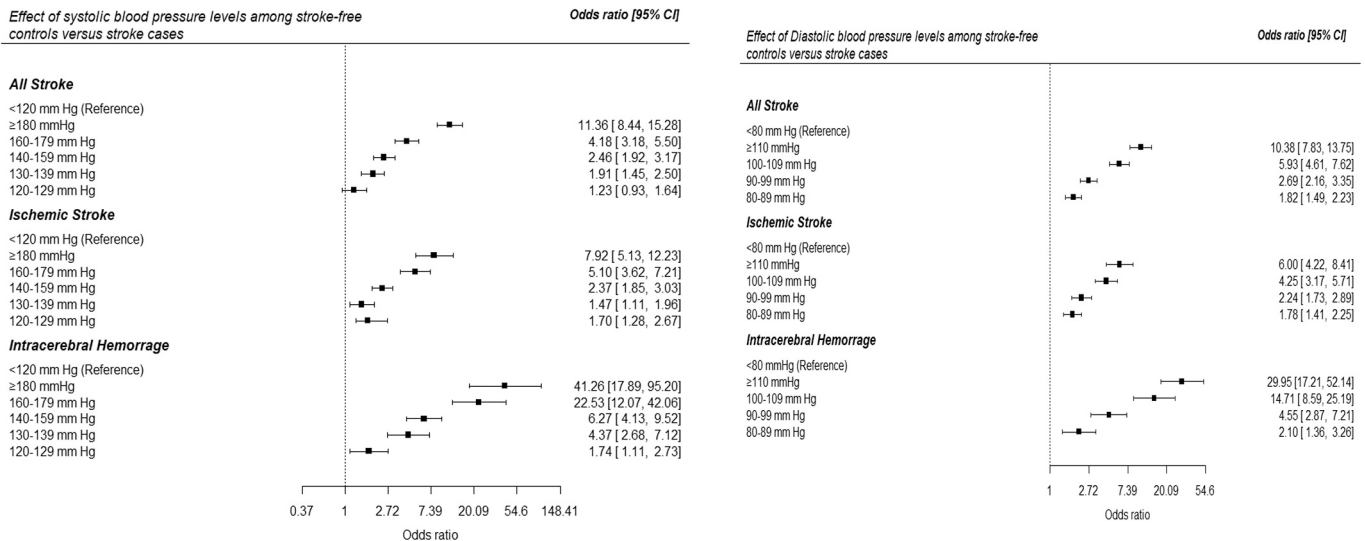


Fig. 4. Systolic & Diastolic BP level with stroke occurrence.

Table 5

Association between Stroke occurrence and premorbid number of antihypertensive classes prescribed.

	All stroke		Ischemic stroke		Intracerebral hemorrhage	
	Adjusted OR (95% CI)	Adjusted PAR (95% CI)	Adjusted OR (95% CI)	Adjusted PAR (95% CI)	Adjusted OR (95% CI)	Adjusted PAR (95% CI)
No prior hypertension or non-hypertensives	ref	ref	ref	ref	ref	ref
No antihypertensive	5.03 (4.05, 6.23)	34.30 (32.05, 36.54)	4.07 (3.12, 5.31)	29.26 (26.33, 32.20)	7.97 (5.39, 11.81)	45.00 (41.55, 48.46)
1 antihypertensive medication	8.95 (6.54, 9.53)	34.30 (32.05, 36.54)	5.89 (4.25, 8.12)	29.26 (26.32, 32.21)	11.02 (6.86, 17.70)	45.00 (41.55, 48.46)
2 antihypertensive medications	8.95 (6.55, 12.22)	13.59 (12.61, 14.57)	9.21 (6.33, 13.40)	15.67 (14.40, 16.96)	7.21 (3.98, 13.09)	8.93 (4.16, 4.85)
3 or more antihypertensive medications	9.09 (5.82, 14.20)	5.34 (4.73, 5.95)	9.86 (5.67, 17.17)	6.23 (5.42, 7.05)	7.12 (3.23, 15.69)	3.42 (2.57, 4.29)

Adjustment for Dyslipidemia, diabetes mellitus, meat consumption, low vegetable consumption, obesity, cardiac disease, cigarette smoking, stress, physical inactivity, table-added salt, age /(>=50), sex, educational attainment (Some), location of residence(urban/semi-urban), monthly income (socio-demographic covariates).

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Data sharing statement

Participant level de-identified data is available with the study PI, MOO, and will be shared with investigators upon request via email to the corresponding author.

CRedit authorship contribution statement

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Declaration of competing interest

We declare no competing interests.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jns.2024.122968>.

References

- [1] D. Ettehad, C.A. Emdin, A. Kiran, et al., Blood pressure lowering for prevention of cardiovascular disease and death: a systematic review and meta-analysis, *Lancet* 387 (2016) 957–967.
- [2] M.J. O'Donnell, S.L. Chin, S. Rangarajan, et al., Global and regional effects of potentially modifiable risk factors associated with acute stroke in 32 countries (INTERSTROKE): a case-control study, *Lancet* 388 (2016) 761–775.
- [3] M.J. O'Donnell, G.J. Hankey, S. Rangarajan, S.L. Chin, P. Rao-Melacini, J. Ferguson, D. Xavier, et al., Variations in knowledge, awareness and treatment of hypertension and stroke risk by country income level, *Heart* 107 (2021) 282–289.
- [4] F. Ataklte, S. Erqou, S. Kaptoge, B. Taye, J.B. Echouffo-Tcheugui, A.P. Kengne, Burden of undiagnosed hypertension in sub-Saharan Africa: a systematic review and meta-analysis, *Hypertension* 65 (2015) 291–298.
- [5] W.K. Bosu, S.T. Reilly, J.M.K. Aheto, E. Zucchelli, Hypertension in older adults in Africa: a systematic review and meta-analysis, *PLoS One* 14 (2019) e0214934.
- [6] O.M. Akpa, F. Made, A. Ojo, B. Ovbiagele, D. Adu, A.A. Motala, et al., Regional patterns and association between obesity and hypertension in Africa: evidence from the Africa CHAIR study, *Hypertension* 75 (2020) 1167–1178.
- [7] G.A. Mensah, U.K.A. Sampson, G.A. Roth, et al., Mortality from cardiovascular diseases in sub-Saharan Africa, 1990–2013: a systematic analysis of data from the global burden of disease study 2013, *Cardiovasc. J. Afr.* 26 (2015) S6–S10.
- [8] M.O. Owolabi, F. Sarfo, R. Akinyemi, M. Gebregziabher, O. Akpa, A. Akpalu, et al., Dominant modifiable risk factors for stroke in Ghana and Nigeria (SIREN): a case-control study, *Lancet Glob. Health* 6 (4) (2018) e436–e446.
- [9] F.S. Sarfo, B. Ovbiagele, O. Akpa, A. Akpalu, K. Wahab, R. Obiako, et al., Risk factor characterization of ischemic stroke subtypes among west Africans, *Stroke* 53 (1) (2022) 134–144.
- [10] A. Akpalu, F.S. Sarfo, B. Ovbiagele, R. Akinyemi, M. Gebregziabher, R. Obiako, et al., Phenotyping stroke in sub-Saharan Africa: stroke investigative research and education network (SIREN) Phenomics protocol, *Neuroepidemiology* 45 (2) (2015) 73–82.
- [11] F. Sarfo, M. Gebregziabher, B. Ovbiagele, R. Akinyemi, L. Owolabi, R. Obiako, O. Akpa, K. Armstrong, A. Akpalu, S. Adamu, et al., Multilingual validation of the questionnaire for verifying stroke-free status in West Africa, *Stroke* 47 (1) (2016) 167–172.
- [12] U. Fischer, M.T. Cooney, L.M. Bull, et al., Acute post-stroke blood pressure relative to pre-morbid level in intracerebral haemorrhage versus major ischemic stroke: a population-based study, *Lancet Neurol.* 13 (4) (2014) 374–384.
- [13] K.G. Alberti, P.Z. Zimmet, Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus provisional report of a WHO consultation, *Diabet. Med.* 15 (1998) 539–553.
- [14] National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment panel). Third report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high cholesterol in adults (adult treatment panel III), *Circulation* 106 (2002), 3143–21.
- [15] World Health Organization, Waist circumference and waist-hip ratio. Report of a WHO expert consultation, 2008. http://www.who.int/nutrition/publications/obesity/WHO_report_waistcircumference_and_waisthip_ratio/en/. Assessed May 27, 2017.
- [16] J. Llorca, Rodriguez M. Delgado-, A comparison of several procedures to estimate the confidence interval for attributable risk in case-control studies, *Stat. Med.* 19 (2000) 1089–1099.
- [17] Dahlqwist E and Sjölander A. AF package-¹Model based estimation of confounder-adjusted attributable fractions. <https://cran.r-project.org/web/packages/AF/index.html>. Assessed May 27, 2017.
- [18] P. Bruzzi, S.B. Green, D.P. Byar, et al., Estimating the population attributable risk for multiple risk factors using case-control data, *Am. J. Epidemiol.* 122 (1985) 904–914.
- [19] F.S. Sarfo, B. Ovbiagele, M. Gebregziabher, K. Wahab, R. Akinyemi, A. Akpalu, et al., Stroke among young west Africans: evidence from the SIREN (stroke investigative research and educational network) large multisite case-control study, *Stroke* 49 (5) (2018) 1116–1122.
- [20] F.S. Sarfo, B. Ovbiagele, M. Gebregziabher, O. Akpa, A. Akpalu, K. Wahab, et al., Unraveling the risk factors for spontaneous intracerebral hemorrhage among west Africans, *Neurology* 94 (10) (2020) e998–e1012.
- [21] B. Williams, G. Mancia, W. Spiering, et al., ESC scientific document group. 2018 ESC/ESH guidelines for the management of arterial hypertension, *Eur. Heart J.* 39 (2018) 3021–3104.
- [22] G. Howard, M. Banach, M. Cushman, D.C. Goff, V. Howard, D.T. Lackland, et al., Is blood pressure control for stroke prevention the correct goal? The lost opportunity of preventing hypertension, *Stroke* 46 (2015) 1595–1600.
- [23] D.A. Lawlor, L. Kim, R. Morris, L. Amuzu, P. Whincup, S. Ebrahim, Survival with treated and well-controlled blood pressure: findings from a prospective cohort study, *PLoS One* 6 (2011) e17792.
- [24] P. Olowoyo, A. Dudzie, AP Okekunle, R. Obiako, A. Mocumbi, H. Beheiry, et al., ACHIEVE conference proceedings: implementing action plans to reduce and control hypertension burden in Africa, *J. Hum. Hypertens.* 38 (3) (2024) 193–199.
- [25] F.S. Sarfo, B. Ovbiagele, Apparent treatment resistant hypertension among stroke survivors in Ghana, *J. Stroke Cerebrovasc. Dis.* 29 (12) (2020) 105401.
- [26] F.S. Sarfo, E. Olasoji, G.P. Banfill, B. Ovbiagele, A.N. Simpkins, Apparent treatment-resistant hypertension among stroke survivors: a transcontinental study assessing impact of race and geography, *Am. J. Hypertens.* 35 (8) (2022) 715–722.
- [27] F.S. Sarfo, J.O. Akinyemi, R. Obiako, M. Nichols, A.G. Fakunle, N. Adusei, et al., Effect of an educational intervention for primary stroke risk reduction in Ghana and Nigeria: pilot randomized controlled trial, *Stroke* (2023) 1660–1664.
- [28] G. Ogedegbe, J. Plange-Rhule, J. Gyamfi, W. Chaplin, M. Ntim, K. Apusiga, et al., Health insurance coverage with or without a nurse-led task shifting strategy for hypertension control: a pragmatic cluster randomized trial in Ghana, *PLoS Med.* 15 (5) (2018) e1002561.
- [29] F.S. Sarfo, O.M. Akpa, B. Ovbiagele, A. Akpalu, K. Wahab, R. Obiako, et al., Patient-level and system-level determinants of stroke fatality across 16 large hospitals in Ghana and Nigeria: a prospective cohort study, *Lancet Glob. Health* 11 (4) (2023) e575–e585.
- [30] F.S. Sarfo, J. Akassi, E. Ofori, B. Ovbiagele, Long-term determinants of death after stroke in Ghana: analysis by stroke types & subtypes, *J. Stroke Cerebrovasc. Dis.* 31 (9) (2022) 106639.