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Influence of age on links between major modifiable risk factors and stroke occurrence in West Africa

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A R T I C L E I N F O

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A B S T R A C T

Background

The burden of stroke in Africa is high. Understanding how age associates with major modifiable stroke risk factors could inform tailored demographic stroke prevention strategies.

Purpose

To quantify the magnitude and direction of the effect sizes of key modifiable stroke risk factors according to three age groups: <50 years (young), 50–65 years (middle age) and > 65 years (elderly) in West Africa.

Methods

This was a case-control study involving 15 sites in Ghana and Nigeria. Cases included adults aged ≥18 years with CT/MRI scan-typed stroke. Controls were age-and gender-matched stroke-free adults. Detailed evaluations for vascular, lifestyle and psychosocial factors were performed. We estimated adjusted odds ratios (aOR) using conditional logistic regression and population attributable risk (PAR) with 95% Confidence Interval of vascular risk factors by age groups.

Results

Among 3553 stroke cases, 813 (22.9%) were young, 1441 (40.6%) were middle-aged and 1299 (36.6%) were elderly. Among the 5 co-shared risk factors, dyslipidemia with PAR and aOR (95%CI) of 62.20% (52.82–71.58) and 4.13 (2.64–6.46) was highest among the young age group; hypertension with PAR of 94.31% (91.82–96.80) and aOR of 28.93 (15.10–55.44) was highest among the middle-age group. Diabetes with PAR of 32.29% (27.52–37.05) and aOR of 3.49 (2.56–4.75); meat consumption with PAR of 42.34%(32.33–52.35) and aOR of 2.40 (1.76, 3.26); and non-consumption of green vegetables, PAR of 16.81%(12.02–21.60) and aOR of 2.23 (1.60–3.12) were highest among the elderly age group. However confidence intervals of risk estimates overlapped across age groups. Additionally, among the young age group cigarette smoking, psychosocial stress and cardiac disease were independently associated with stroke. Furthermore, education, stress, physical inactivity

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and salt intake were associated with stroke in the middle-age group while cardiac disease was associated with stroke in the elderly age group.

Conclusion

There is a differential influence of age on the associations of major risk factors with stroke in this West African cohort. Targeting modifiable factors predominant within an age group may be more effective as a stroke prevention strategy.

1. Introduction

Incidence of stroke increases sharply with age due to clustering of cardio-metabolic risk factors [1].Stroke can however occur at any age exerting heavy personal, family and societal tolls. In sub-Saharan Africa, there is an unprecedented rise in the incidence, prevalence, morbidity and mortality of stroke [2]. On a continent with a population of 1 billion, stroke affects an individual every 6 min, disproportionately falling on the young and middle-age populations. A lack of awareness, detection and control of risk factors for stroke occurrence is pervasive and appears to be a strong driver of this public health challenge [3,4].

To develop population wide preventative strategies to curtail stroke in Africa, a clearer resolution of the magnitude of the contribution of vascular risk factors to stroke occurrence across the lifespan is essential. To date, very few large scale, representative studies have hitherto been conducted in Africa to provide context-specific data to guide efforts at stroke prevention. Specifically, there are important gaps in our understanding on the dispersion of vascular risk factors for stroke occurrence by epidemiologically relevant age categories in Africa. This information is needed as a critical strategic step in our preparations towards developing, tailoring, testing, and scaling up of population wide stroke prevention interventions in Africa. Our rationale for this study was therefore to examine the qualitative and quantitative relationships of major modifiable vascular risk factors to stroke and its subtypes by major age categories in large West African sample. We analyzed the associations of stroke risk factors in three main categories by age namely <50 years (young), 50–64 years (middle aged) and ≥ 65 years (the elderly).

2. Methods

2.1. Study design

The SIREN study is a multicenter case-control study involving 15 medical centers in Ghana and Nigeria. A detailed protocol has been previously published [5]. We recruited consenting CT scan-confirmed *stroke cases* who were ≥ 18 years old with first clinical stroke within 8 days of current symptom onset or 'last seen without deficit'. Valid proxies provided consent for stroke cases who were aphasic or unconscious at enrollment. Stroke cases were phenotyped into ischemic and intracerebral hemorrhage (ICH) primary types, ischemic strokes were etiologically subtyped into cardio-embolic, large artery atherosclerotic disease and small vessel occlusive disease. We recruited *stroke-free controls*, mostly from the communities in the catchment areas of the SIREN hospitals using outreach programs at each site. Controls were matched to cases by age (+/− 5 years), sex and ethnicity, to reduce the potential for confounding from these variables. Ethical approval was obtained from all study sites and informed consent was obtained from all participants.

2.2. Data collection

Basic demographic, socioeconomic, lifestyle (including cigarette smoking and alcohol use), physical activity, dietary, 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 and fasting glucose were obtained following a uniform standard operating procedure across all study sites.

2.3. Definition of risk factors

- Hypertension: An average of three blood pressure (BP) measurements was obtained at baseline and daily for 7 days or until death [6]. Hypertension was defined using a cutoff of ≥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 pre-morbid hypertensive status or were either aphasic or unconscious to provide information on history of hypertension. Hence diagnosis of hypertension relied on BP measurements taken after ICH and to account for elevations in post-stroke BP in relation to pre-morbid BP, we made adjustments to systolic BP (SBP) by applying a correction factor of 0.8755 to SBPs measured in accordance with recommendations of the Oxford Vascular Study (OXVASC) in sensitivity analyses [7]. In controls, hypertension was defined as self-reported history of hypertension or use of antihypertensive drugs or average BP at first clinical encounter ≥140/90 mmHg [6].
- Dysglycemia: Diabetes mellitus (DM) was defined using either a history of diabetes mellitus, use of medications for DM, an elevated HBA1c ≥6.5% or a fasting blood glucose (FBG) levels ≥7.0 mmol/l for controls or FBG taken after 7 days for stroke cases due to stress-induced transient rise in plasma glucose [8]. Euglycemia/normoglycemia was defined as HBA1c <5.7% or Fasting blood glucose <5.6 mmol/l; Pre-diabetes/impaired glucose tolerance: HBA1c 5.7%–6.4% or Fasting blood glucose 5.6–7.0 mmol/l.
- 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 [9] or use of statin prior to stroke onset. The LDL/HDL ratio was categorized into the lowest two tertiles (≤1.97 and 1.98–2.95) as normal and compared with the highest tertile (≥2.96) based on distribution of the LDL/HDL ratio in our study.
- Cardiac disease was defined on the basis of either a history, clinical examination and E.C.G. or echocardiographic evidence of atrial fibrillation, heart failure, ischemic heart disease, cardiomyopathy, rheumatic heart disease, or valvular heart diseases.
- 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/m^2 were classified as obese using World Health Organization cut-offs [10].
- 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 [6].
- Dietary history: The regularity of consumption of food items such as green leafy vegetables, addition of salt at 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. Regular consumption was categorized using daily or weekly consumption while low consumption was categorized using at least once monthly and none in a month.
- 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 female) and high if consumption exceeded these sex-specific cut-offs. [6]

- 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.
- Psychosocial factors such as psychosocial stress and depression were assessed using validated instruments from the INTERSTROKE study [6]. Combined measures of psychosocial stress at home or work such as anxiety, sleeping difficulties or irritability and life events experienced in the preceding 2 weeks of stroke onset were used to define presence of stress. The presence of depression was screened for using a combined checklist of depression symptoms experienced in the 4 weeks before stroke.
- Family history of cardiovascular diseases (CVD) was defined on the basis of self-reported history of any of hypertension, dyslipidemia, diabetes, stroke, cardiac disease or obesity in participants' father, mother, sibling or second degree relative.

2.4. Statistical analysis

We compared demographic characteristics and risk factors for stroke according to the age categories (<50 years, 50–64 years, and 65+ years) using either Analysis of variance (ANOVA) for more than two group comparisons of continuous variables or Chi-squared test for categorical variables. We used conditional logistic regression models to determine the adjusted associations between stroke, its types and risk factors. Adjustments were made for potential confounders not used in the matching except baseline age which was included due to the non-exact age matching. The final adjusted models were assessed for collinearity using 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 stroke for each risk factor included in the best-fitted adjusted models were determined. We calculated the 95%CI for the PARs using the AF R-package [11] and estimated the variance using the delta method. Composite PARs for the risk factors for ICH and subtypes of ischemic stroke were calculated using the ATTRIBRISK R package with its 95% CI computed via the bootstrap method [12]. 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).

3. Results

3.1. Comparison of stroke cases with controls

Over the period of the study, 7000 suspected stroke cases presented at the 15 study sites out of which 3553 were enrolled and 3447 were excluded. The reasons for exclusion include not having a head CT scan to confirm stroke diagnosis ($n = 2950$) and presenting with symptoms that had lasted >10 days before head CT scan was taken making difficult to ascertain whether stroke was ischemic or hemorrhagic ($n = 497$). Table 1 shows a comparison of key demographic and vascular risk factors of stroke cases and controls.

3.2. Distribution of stroke types and sub-types by age categories

Among the 3553 stroke cases out of which 813 (22.9%) were < 50 years old, 1441 (40.6%) were between 50 and 64 years, and 1229 (34.6%) were ≥ 65 years. The distribution of stroke types (intracerebral hemorrhage vs. ischemic stroke) and etiologic subtypes of ischemic stroke namely large artery atherosclerosis, small vessel occlusive disease and cardio-embolic strokes by age categories is shown in Fig. 1. Among stroke cases, 2132 (60.0%) had electrocardiography, 1335 (37.5%) had echocardiography done, and 1249 (33.1%) had carotid doppler ultrasound performed. However, none of the controls had these three investigations performed.

Table 1
Comparison of stroke cases with controls.

Variable	Stroke status		p-Value
	Control	Case	
	($n = 3553$)	($n = 3553$)	
Gender, Male, % [1]	1942 (54.7)	1939 (54.6)	0.922
Age, mean ± SD	58.71 ± 13.95	59.17 ± 13.93	0.445
Monthly Income >$100, %	1340 (37.7)	1910 (53.8)	<0.001
Education, (some) %	2751 (77.4)	2879 (81.0)	<0.001
Hypertension, %	2093 (58.9)	3361 (94.6)	<0.001
Dyslipidemia, %	1931 (54.3)	2913 (82.0)	<0.001
Diabetes, %	403 (11.3)	1322 (37.2)	<0.001
Cardiac Disease, %	154 (4.3)	414 (11.7)	<0.001
Waist-to-hip Ratio raised, %	2432 (68.4)	2687 (75.6)	<0.001
BMI*** > 30 kg/m^2, %	730 (20.5)	593 (16.7)	0.984
Physical Inactivity, %	79 (2.2)	166 (4.7)	<0.001
Tobacco use in past 12 months, %	46 (1.3)	121 (3.4)	<0.001
Tobacco (any use), %	254 (7.1)	334 (9.4)	<0.001
Alcohol (current user), %	493 (13.9)	575 (16.2)	0.003
Alcohol (any use), %	997 (28.1)	1108 (31.2)	0.001
Stress, %	467 (13.1)	652 (18.4)	<0.001
Cancer, %	3 (0.1)	22 (0.6)	<0.001
Depression, %	197 (5.5)	253 (7.1)	<0.001
Family history of CVD, %	913 (25.7)	1330 (37.4)	<0.001
Adding salt at table, %	282 (7.9)	232 (6.5)	0.059
Low vegetable consumption, %	592 (16.7)	859 (24.2)	<0.001
Whole grains consumption, %	2924 (82.3)	2741 (77.1)	0.705
Legumes consumption, %	2165 (60.9)	2180 (61.4)	0.001
Fruit consumption, %	2973 (83.7)	2742 (77.2)	0.037
Sugar consumption or otherwise, %	1158 (32.6)	942 (26.5)	<0.001
Regular Meat consumption %	2352 (66.2)	2431 (68.4)	<0.001
Fish consumption or otherwise, %	3161 (89.0)	2983 (84.0)	0.810

3.3. Vascular risk factor profile of stroke cases by age categories

The distribution of key vascular risk factors across the age categories are shown in Fig. 2 and summarized in Table 2. The prevalence of some of the risk factors such as hypertension, dyslipidemia, diabetes, central obesity tended to increase with increasing age. The frequency distribution of cardiac diseases however followed a U-shaped age distribution with age < 30 years having the highest burden and an inflection point at 30–49 years. Supplementary table S1 shows distribution of demographic and vascular risk factors for ischemic stroke, S2 (ICH), S3 (lacunar strokes), S4 (large artery atherosclerotic disease) and S5 (cardio-embolic strokes). Prior to onset of stroke, 523 (14.7%) were on antiplatelets, 212 (6.0%) were on statins and 38 (1.1%) were on anticoagulants with usage of these medication increasing with age (Table 3).

3.4. Modifiable risk factors for stroke occurrence by age

Five factors namely hypertension, dyslipidemia, diabetes mellitus, meat consumption, and low vegetable consumption were independently associated with stroke occurrence across the young ages (<50 years), middle age (50–64 years) and older ages (≥65 years) as shown in Table 4 and Fig. 3. The adjusted PAR and OR of hypertension for stroke occurrence was highest among the 50–64-year group, being 94.31% (91.82–96.80) and 28.93 (15.10–55.44), respectively. PAR and OR for dyslipidemia was highest among the <50-year group, being 62.20% (52.82–71.58) and 4.13 (2.64–6.46) respectively, and diabetes was highest among the ≥65-year group, PAR of 32.29% (27.52–37.05) and aOR of 3.49 (2.56–4.75). The highest effect sizes for meat consumption and low vegetable consumption were noted among the ≥65-year group. Among the young (<50 years), additional factors independently associated with stroke were cardiac diseases, cigarette smoking, and psychosocial stress. Four additional factors independently associated with

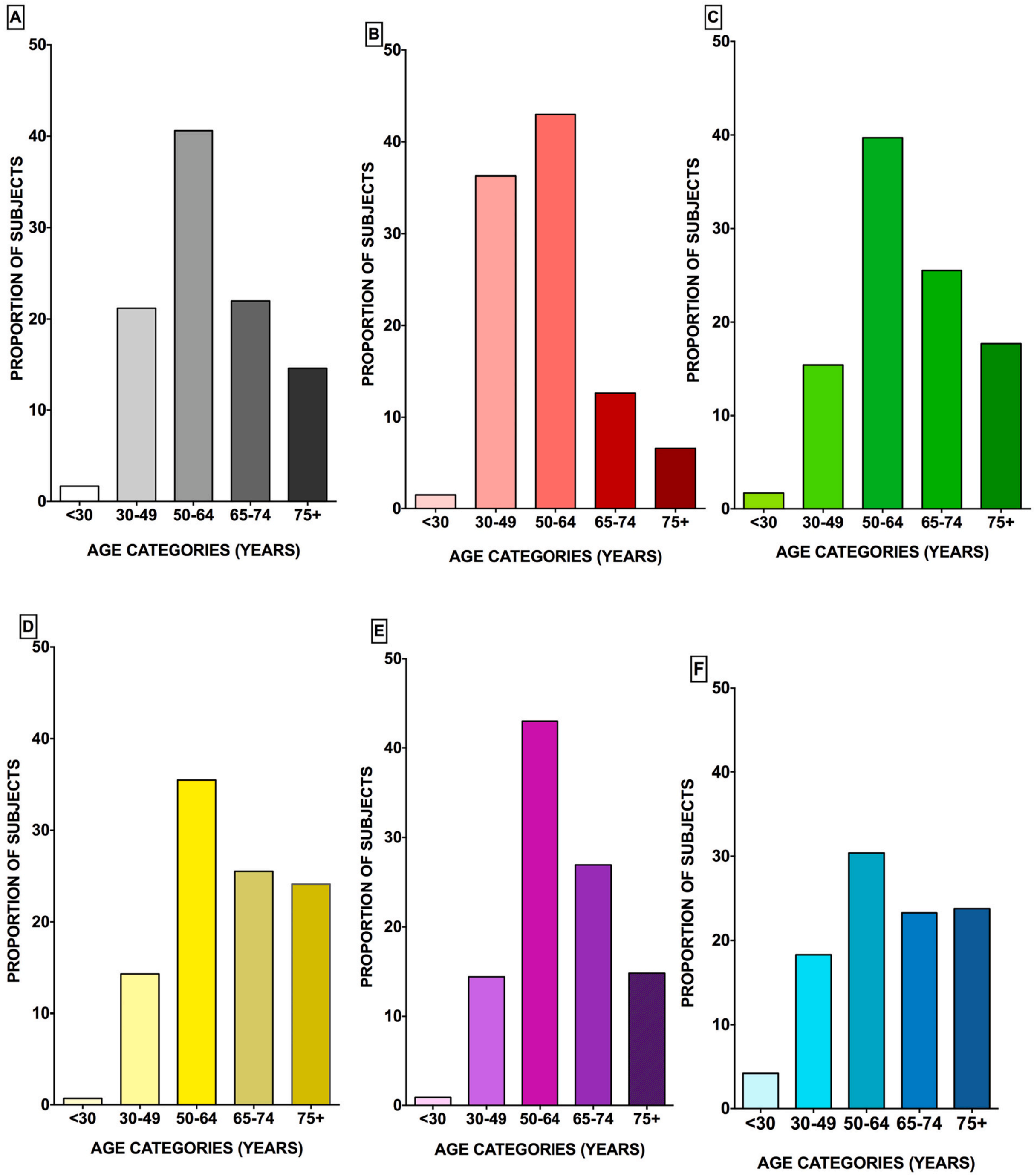

Fig. 1. Age frequency distribution of (A) all strokes, (B) Intracerebral hemorrhage, (C) Ischemic strokes, (D) Large artery atherosclerotic ischemic strokes, (E) Small vessel occlusive ischemic strokes, (F) Cardio-embolic strokes.

stroke occurrence in the middle age group were educational attainment, psychosocial stress, physical inactivity and adding salt at table. Finally, cardiac disease was independently associated with stroke occurrence among those older than 64 years.

3.5. Effect sizes of modifiable risk factors for stroke type occurrence by age

Three factors namely hypertension, dyslipidemia, and diabetes mellitus are independently associated with occurrence of ischemic stroke across the age groups shown in Table 4. Hypertension and regular meat consumption are factors independently associated with spontaneous intracerebral hemorrhage across the age groups (Table 4).

4. Discussion

In our initial report involving 2118 stroke case-control pairs, we identified 11 dominant risk factors associated with stroke occurrence in West Africa [13]. We have since updated our sample size to 3553 case-control pairs to focus the current analysis on the dispersion of stroke risk factors by age strata. Five factors namely hypertension, dyslipidemia, diabetes mellitus, regular meat consumption, and low vegetable consumption were independently associated with stroke occurrence across all the lifespan. Our study highlights the significant and novel

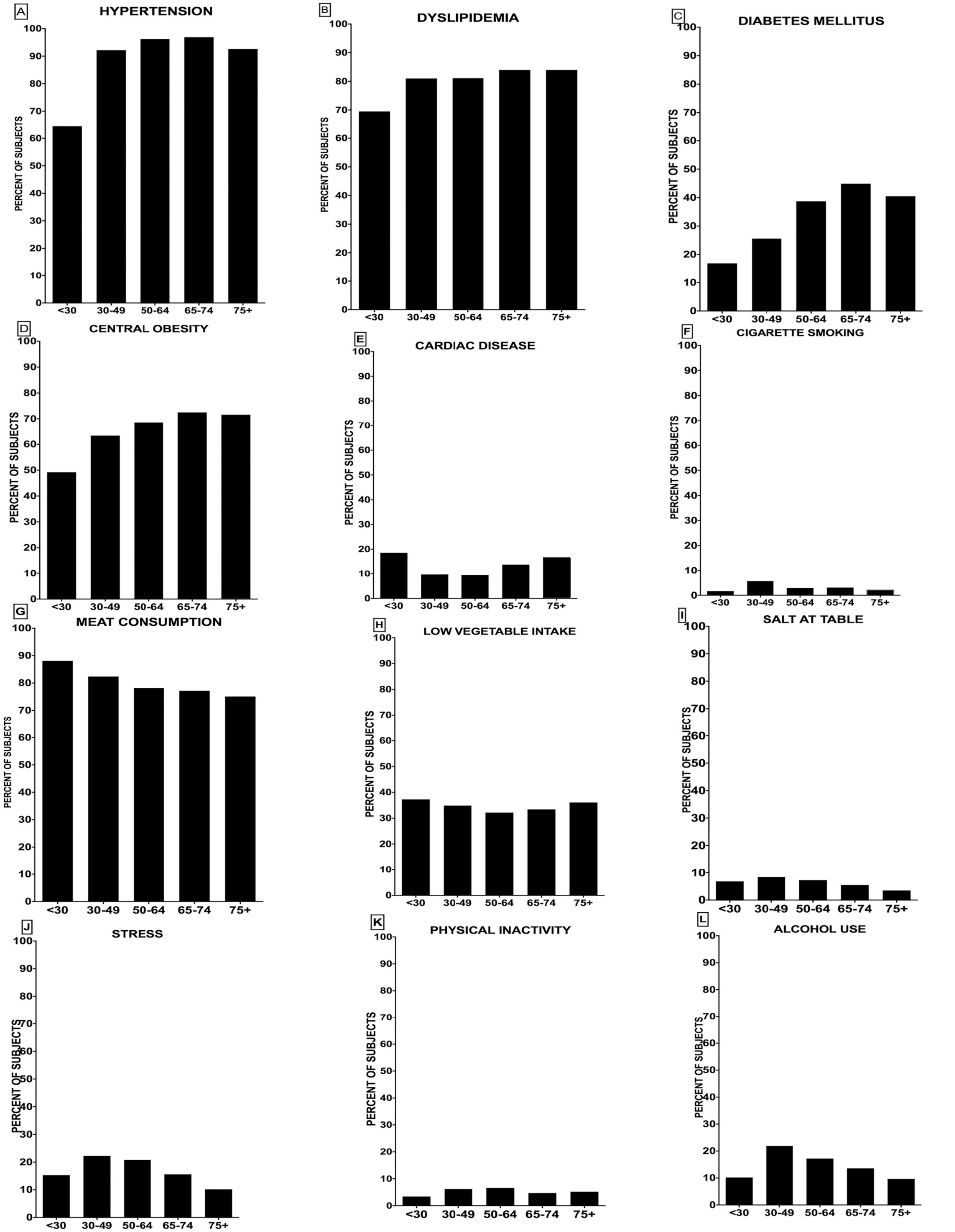

Fig. 2. Distribution of vascular risk factors among stroke cases by 5 age strata.

Table 2
Frequencies of vascular risk factors for Stroke by three age categories.

Characteristic	Age < 50 years $N = 813$	Age 50–64 years $N = 1441$	Age ≥ 65 years $N = 1299$	*p*-Value
Country, Ghana, *n* (%)	298 (36.65)	455 (31.58)	371 (28.56)	<0.001
Gender, Male, *n* (%)	446 (54.86)	815 (56.56)	678 (52.19)	0.071
Domicile				
Rural, *n* (%)	47 (5.78)	116 (8.05)	149 (11.47)	<0.001
Semi-urban, *n* (%)	236 (29.03)	426 (29.56)	378 (29.10)	
Urban, *n* (%)	526 (64.70)	893 (61.97)	767 (59.05)	
Monthly Income >$100, *n* (%)	459 (56.46)	853 (59.20)	598 (46.04)	<0.001
Education, (some) *n* (%)	747 (91.88)	1254 (87.02)	878 (67.59)	<0.001
Hypertension, *n* (%)	733 (90.16)	1386 (96.18)	1242 (95.61)	<0.001
Dyslipidemia, *n* (%)	652 (80.20)	1169 (81.12)	1091 (83.99)	0.018
Diabetes	203 (24.97)	558 (38.72)	561 (43.19)	<0.001
Cardiac Disease, *n* (%)	84 (10.33)	135 (9.37)	195 (15.01)	<0.001
Atrial fibrillation, *n* (%)	5 (0.62)	9 (0.62)	16 (1.23)	0.224
Waist-to-hip Ratio raised, *n* (%)	582 (71.59)	1101 (76.41)	1004 (77.29)	0.003
BMI (kg/m^2), mean ± SD	26.73 ± 5.76	26.86 ± 5.49	25.79 ± 5.46	<0.001
BMI > 30 kg/m^2, *n* (%)	145 (17.84)	241 (16.72)	207 (15.94)	0.380
Physical Inactivity), *n* (%)	26 (3.20)	50 (3.47)	90 (6.93)	<0.001
Tobacco (any use), *n* (%)	70 (8.61)	133 (9.23)	131 (10.08)	0.484
Alcohol use categories:				
Never Use, *n* (%)	538 (66.17)	938 (65.09)	899 (69.21)	<0.001
Ever Low Use, *n* (%)	149 (18.33)	275 (19.08)	188 (14.47)	
Ever High Use, *n* (%)	32 (3.94)	41 (2.85)	19 (1.46)	
Stress, *n* (%)	177 (21.77)	300 (20.82)	175 (13.47)	<0.001
Cancer, *n* (%)	2 (0.25)	9 (0.62)	11 (0.85)	0.167
Depression, *n* (%)	66 (8.12)	109 (7.56)	78 (6.00)	0.358
Family history of CVD, *n* (%)	332 (40.84)	563 (39.07)	435 (33.49)	0.001
Adding salt at table, *n* (%)	67 (8.24)	104 (7.22)	61 (4.70)	0.002
Low vegetable consumption, *n* (%)	211 (25.95)	342 (23.73)	306 (23.56)	0.421
Whole grains consumption, *n* (%)	630 (77.49)	1129 (78.35)	982 (75.60)	0.718
Legumes consumption, *n* (%)	514 (63.22	918 (63.71)	748 (57.58)	0.028
Fruit consumption, *n* (%)	623 (76.63)	1140 (79.11)	979 (75.37)	0.205
Sugar consumption or otherwise, *n* (%)	293 (36.04)	403 (27.97)	246 (18.94)	<0.001
Regular Meat consumption %	595 (73.19)	971 (67.38)	865 (66.59)	0.006
Fish consumption or otherwise, %	692 (85.12)	1218 (84.52)	1073 (82.60)	0.410
ECG	521 (64.08)	874 (64.08)	737 (56.74)	0.003
Echo	314 (38.62)	534 (37.06)	487 (37.49)	0.76
Carotid Doppler	309 (38.01)	510 (35.39)	430 (33.10)	0.06

contribution of dietary practices namely meat and vegetable consumption on the occurrence of stroke across the various age categories in Africa. Although ≈ 25% of stroke cases were young (<50 years), 40% were middle aged (50–64 years) and 35% were elderly (≥65 years), stroke types and etiologic subtypes were differentially distributed across the adult lifespan.

Table 3
Frequency of use of preventative cardiovascular medications prior to stroke onset.

	All stroke				
	Age < 50 years $N = 813$	Age 50–64 years $N = 1441$	Age ≥ 65 years $N = 1299$	Total $N = 3553$	*p*-Value
Antiplatelets	62 (7.63)	233 (16.17)	228 (17.55)	523 (14.72)	<0.001
Anticoagulants	7 (0.76)	11 (0.76)	20 (1.54)	38 (1.07)	0.10
Statins	28 (3.44)	79 (5.48)	105 (8.08)	212 (5.97)	<0.001
	Ischemic stroke				
	Age < 50 years $N = 377$	Age 50–64 years $N = 874$	Age ≥ 65 years $N = 952$	Total $N = 2203$	*p*-Value
Antiplatelets	39 (10.34)	173 (12.01)	176 (18.49)	388 (17.61)	<0.001
Anticoagulants	7 (1.86)	8 (0.56)	16 (1.68)	31 (1.41)	0.27
Statins	13 (3.45)	61 (4.23)	82 (8.61)	156 (7.08)	0.004
	Intracerebral hemorrhage				
	Age < 50 years $N = 354$	Age 50–64 years $N = 403$	Age ≥ 65 years $N = 180$	Total $N = 937$	*p*-Value
Antiplatelets	12 (3.39)	38 (9.43)	17 (9.44)	67 (7.15)	0.002
Anticoagulants	0 (0.0)	2 (0.50)	2 (1.11)	4 (0.43)	0.19
Statins	5 (1.41)	9 (2.23)	9 (5.00)	23 (2.45)	0.04

There were about equal proportions of ischemic and hemorrhagic strokes in the young. Ischemic strokes are still the dominant stroke type among the young in high-income countries compared with that in Africa [14]. The 6 factors which were associated with ICH by PAR were hypertension, dyslipidemia, regular meat consumption, alcohol consumption, cigarette smoking, and adding salt at table. A sub-analysis of INTERSTROKE study among 4216 case-control pairs <55 years showed that the 10 factors identified in their overall analysis, accounting for a PAR of 92.2% for stroke occurrence in the young across the globe [15]. Therefore the spectrum, magnitude and direction of effect sizes of risk factors for stroke occurrence in the young are becoming increasingly similar to those of the older age group [16].

The bulk of adult strokes in Africa occur in the middle ages. Here, we find the widest array of vascular risk factors associated with stroke occurrence. Nine of the 13 factors assessed were associated with stroke in this age group overall, with 8 of them associated with ischemic strokes and 7 with ICH. In addition, the major stroke types and sub-types of ischemic stroke have their peak occurrence in this age group. Among the elderly population, we observed a sharp decline in proportion of ICH with a rise in ischemic stroke. This is similar to the stroke epidemiology in high-income countries. Although, the frequency of atrial fibrillation (AF) was surprisingly very low in our study, the frequency of AF was highest in our elderly population at <2%. This low rate of AF could be due to lack of continuous E.K.G. monitoring after stroke and low detection of AF prior to stroke occurrence and require further studies.

Table 4
Dispersion of factors associated with stroke occurrence across the adult lifespan by stroke types. The bold signifies Composite Population Attributable Risk

Risk factor	All strokes					
	Age <50 years		Age 50–64 years		Age ≥ 65 years	
	Adjusted OR (95%CI)	PAR (95% CI)	Adjusted OR (95% CI)	PAR (95% CI)	Adjusted OR (95% CI)	PAR (95% CI)
Educational attainment	1.91 (0.92, 3.93)	44.17 (1.15, 87.19)	1.54 (1.06, 2.23)	30.58 (9.26, 51.91)	1.29 (0.93, 1.80)	15.87 (−2.84, 34.58)
Hypertension	16.75 (9.80, 28.63)	85.36 (81.88, 88.84)	28.93 (15.10, 55.44)	94.31 (91.82, 96.80)	10.88 (6.50, 18.22)	87.69 (83.00, 92.39)
Dyslipidemia	4.13 (2.64, 6.46)	62.20 (52.82, 71.58)	3.95 (2.90, 5.39)	61.71 (55.01, 68.41)	3.50 (2.48, 4.95)	61.88 (53.29, 70.47)
Diabetes mellitus	3.29 (1.76, 6.16)	17.27 (12.16, 22.39)	2.80 (2.09, 3.76)	24.04 (19.48, 28.60)	3.49 (2.56, 4.75)	32.29 (27.52, 37.05)
Cigarette smoking	4.05 (1.00, 16.44)	4.41 (2.19, 6.62)	2.18 (0.87, 5.42)	1.52 (0.24, 2.80)	2.03 (0.75, 5.51)	1.06 (−0.24, 2.36)
Stress	1.70 (1.00, 2.89)	9.95 (2.46, 17.45)	1.90 (1.33, 2.73)	11.01 (6.25, 15.77)	1.09 (0.73, 1.63)	1.29 (−4.51, 7.10)
Cardiac disease	4.36 (1.82, 10.40)	7.24 (5.01, 9.47)	1.24 (0.75, 2.05)	1.66 (−1.97, 5.29)	2.41 (1.47, 3.96)	8.40 (4.92, 11.89)
Alcohol	1.34 (0.81, 2.21)	8.47 (−3.94, 20.89)	1.03 (0.76, 1.40)	1.11 (−9.23, 11.45)	1.06 (0.75, 1.50)	1.66 (−9.21, 12.52)
Meat consumption	1.63 (1.02, 2.61)	31.25 (7.01, 55.49)	1.79 (1.34, 2.40)	32.09 (20.16, 44.01)	2.40 (1.76, 3.26)	42.34 (32.33, 52.35)
Low Vegetable consumption	1.70 (1.04, 2.77)	12.02 (3.25, 20.79)	2.34 (1.70, 3.23)	15.62 (11.32, 19.91)	2.23 (1.60, 3.12)	16.81 (12.02, 21.60)
Depression	1.26 (0.55, 2.89)	1.84 (−3.40, 7.08)	0.70 (0.42, 1.15)	−3.72 (−9.96, 2.52)	0.98 (0.52, 1.83)	−0.15 (−4.34, 4.04)
Physical inactivity	3.53 (0.92, 13.47)	2.29 (0.87, 3.70)	2.97 (1.12, 7.87)	2.20 (0.82, 3.58)	0.87 (0.49, 1.54)	−0.93 (−5.24, 3.37)
Salt intake	1.25 (0.63, 2.50)	1.82 (−2.90, 6.53)	1.65 (1.00, 2.73)	3.10 (0.79, 5.41)	1.13 (0.62, 2.09)	0.66 (−2.32, 3.63)
Composite PAR		**85.68 (78.00, 93.61)**		**94.60 (91.16, 98.04)**		**94.33 (91.42, 97.24)**
Ischemic stroke						
Educational attainment	3.05 (1.05, 8.89)	61.98 (24.01, 99.94)	1.99 (1.21, 3.28)	42.66 (19.97, 65.36)	1.22 (0.87, 1.80)	12.47 (−8.40, 33.35)
Hypertension	7.97 (3.95, 16.09)	73.11 (64.59, 81.62)	22.52 (9.36, 54.20)	92.96 (88.53, 97.40)	8.83 (5.01, 15.53)	85.42 (79.19, 91.65)
Dyslipidemia	7.92 (3.85, 16.28)	77.47 (68.40, 86.54)	6.64 (4.17, 10.58)	73.83 (67.50, 80.17)	3.94 (2.59, 5.98)	65.04 (55.61, 74.47)
Diabetes mellitus	5.05 (1.77, 14.40)	20.68 (15.09, 26.27)	3.45 (2.33, 5.10)	29.89 (24.22, 35.55)	3.75 (2.60, 5.41)	35.26 (29.68, 40.84)
Cigarette smoking	1.70 (0.29, 9.98)	1.94 (−2.34, 6.21)	3.30 (0.68, 15.99)	1.66 (0.57, 2.74)	1.23 (0.38, 3.97)	0.34 (−1.50, 2.19)
Stress	1.75 (0.82, 3.73)	12.22 (−0.03, 24.47)	2.03 (1.22, 3.36)	12.38 (5.63, 19.13)	1.06 (0.65, 1.71)	0.85 (−6.48, 8.18)
Cardiac disease	12.77 (2.97, 54.99)	11.52 (9.00, 14.05)	1.08 (0.55, 2.13)	0.76 (−5.78, 7.30)	2.91 (1.65, 5.15)	10.71 (6.81, 14.61)
Alcohol	0.62 (0.27, 1.43)	−16.83 (−50.40, 16.74)	0.98 (0.64, 1.51)	−0.54 (−14.73, 13.65)	0.99 (0.66, 1.48)	−0.31 (−14.46, 13.84)
Meat consumption	1.69 (0.84, 3.41)	31.91 (−4.15, 67.96)	1.86 (1.24, 2.77)	32.82 (17.64, 48.01)	2.23 (1.55, 3.20)	38.38 (26.69, 50.08)
Low Vegetable consumption	1.69 (0.79, 3.63)	10.21 (−3.46, 23.88)	2.47 (1.59, 3.83)	15.36 (10.17, 20.54)	2.17 (1.46, 3.22)	16.24 (10.57, 21.91)
Depression	1.22 (0.35, 4.30)	1.82 (−9.96, 13.59)	0.85 (0.43, 1.71)	−1.64 (−8.83, 5.56)	0.94 (0.47, 1.89)	−0.46 (−5.84, 4.92)
Physical inactivity	9.03 (0.31, 262.02)	0.69 (0.12, 1.27)	3.75 (1.08, 12.99)	2.62 (1.07, 4.16)	0.90 (0.47, 1.72)	−0.76 (−6.25, 4.72)
Salt intake	0.73 (0.26, 2.09)	−2.69 (−12.14, 6.75)	1.76 (0.80, 3.90)	3.01 (−0.02, 6.05)	1.11 (0.56, 2.20)	0.55 (−3.12, 4.21)
Composite PAR		**83.50 (68.49, 98.51)**		**94.38 (90.01, 98.76)**		**93.79 (89.82, 97.76)**
Intracerebral hemorrhage						
Educational attainment	0.99 (0.30, 3.33)	−0.60 (−106.21, 105.02)	0.67 (0.31, 1.44)	−44.58 (−139.86, 50.70)	1.25 (0.55, 2.86)	14.93 (−42.76, 72.61)
Hypertension[a]	50.39 (15.97, 158.97)	88.79 (85.59, 91.99)	23.26 (9.25, 58.46)	92.52 (87.98, 97.06)	5.95 (2.08, 16.99)	75.37 (58.40, 92.33)
Dyslipidemia	2.82 (1.30, 6.13)	50.39 (28.50, 72.27)	2.78 (1.58, 4.88)	51.26 (35.34, 66.67)	2.22 (0.91, 5.41)	45.49 (13.60, 77.37)
Diabetes mellitus	2.46 (0.90, 6.71)	13.73 (3.49, 23.97)	2.25 (1.30, 3.91)	16.25 (8.28, 24.23)	1.72 (0.82, 3.61)	12.19 (−0.97, 25.35)
Cigarette smoking	104.61 (5.71, 1915.12)	7.77 (6.10, 9.44)	1.04 (0.27, 3.91)	0.13 (−3.99, 4.25)	5.17 (0.48, 56.08)	3.45 (0.14, 6.75)
Stress	0.79 (0.32, 1.95)	−5.32 (−26.64, 16.00)	2.95 (1.54, 5.65)	16.26 (10.42, 22.10)	0.93 (0.37, 2.36)	−0.93 (−12.54, 10.69)
Cardiac disease	0.79 (0.17, 3.73)	−1.58 (−12.41, 9.25)	1.79 (0.65, 4.91)	2.78 (−1.29, 6.86)	1.25 (0.33, 4.75)	1.69 (−6.20, 9.57)
Alcohol	3.39 (1.42, 8.08)	30.13 (17.18, 43.09)	1.27 (0.76, 2.11)	9.51 (−8.33, 27.35)	1.77 (0.73, 4.27)	14.09 (−2.64, 30.81)
Meat consumption	2.57 (1.18, 5.61)	49.10 (26.05, 72.15)	1.75 (1.06, 2.91)	30.28 (7.89, 52.67)	2.09 (1.02, 4.31)	38.84 (12.73, 64.95)
Low Vegetable consumption	1.96 (0.80, 4.80)	15.91 (2.11, 29.70)	2.81 (1.50, 5.25)	19.24 (10.79, 27.69)	2.94 (1.26, 6.85)	23.11 (11.75, 34.46)
Depression	2.22 (0.45, 11.12)	4.53 (−2.70, 11.76)	0.80 (0.35, 1.83)	−2.43 (−12.63, 7.77)	1.13 (0.16, 8.08)	0.39 (−5.52, 6.30)
Physical inactivity	1.10 (0.23, 5.31)	0.40 (−5.71, 6.51)	0.72 (0.12, 4.24)	−1.29 (−8.64, 6.05)	0.70 (0.08, 5.82)	−0.75 (−6.20, 4.70)
Salt intake	3.72 (1.10, 12.58)	7.46 (3.52, 11.40)	2.58 (1.10, 6.03)	6.72 (3.14, 10.29)	1.71 (0.31, 9.39)	3.20 (−1.74, 8.14)
Composite PAR		**86.07 (73.32, 98.82)**		**90.06 (80.95, 99.17)**		**78.53 (59.62, 97.44)**

[a] Hypertension was defined as previous diagnosis by a healthcare professional or use of hypertension medication or systolic blood pressure ≥140 mmHg or a combination of these.

4.1. Implications

Health promotion to enhance the awareness of the public to the dire effects of undiagnosed hypertension and other vascular risk factors should be intensified via media channels and portals. Mobile technology may prove to be an effective vehicle for dissemination given its high penetration in SSA. The institution of healthy lifestyle modification including healthy weight and healthy diets, for primordial, primary and secondary stroke prevention should be vigorously pursued [17–19]. Another major challenge with stroke prevention in Africa is a lack of an Afrocentric stroke prediction model. Therefore, developing lifetime stroke risk prediction models for Africans instead of short-term (5-year or 10-year) total CVD risk [20] should be prioritized given the significant burden of risk factors which occur at a younger age.

The most appropriate strategy for cardiovascular risk mitigation remains to be determined in reaching the population in Africa. A population-based approach where individuals are screened for the dominant risk factors by age strata and treated may be cost-effective.

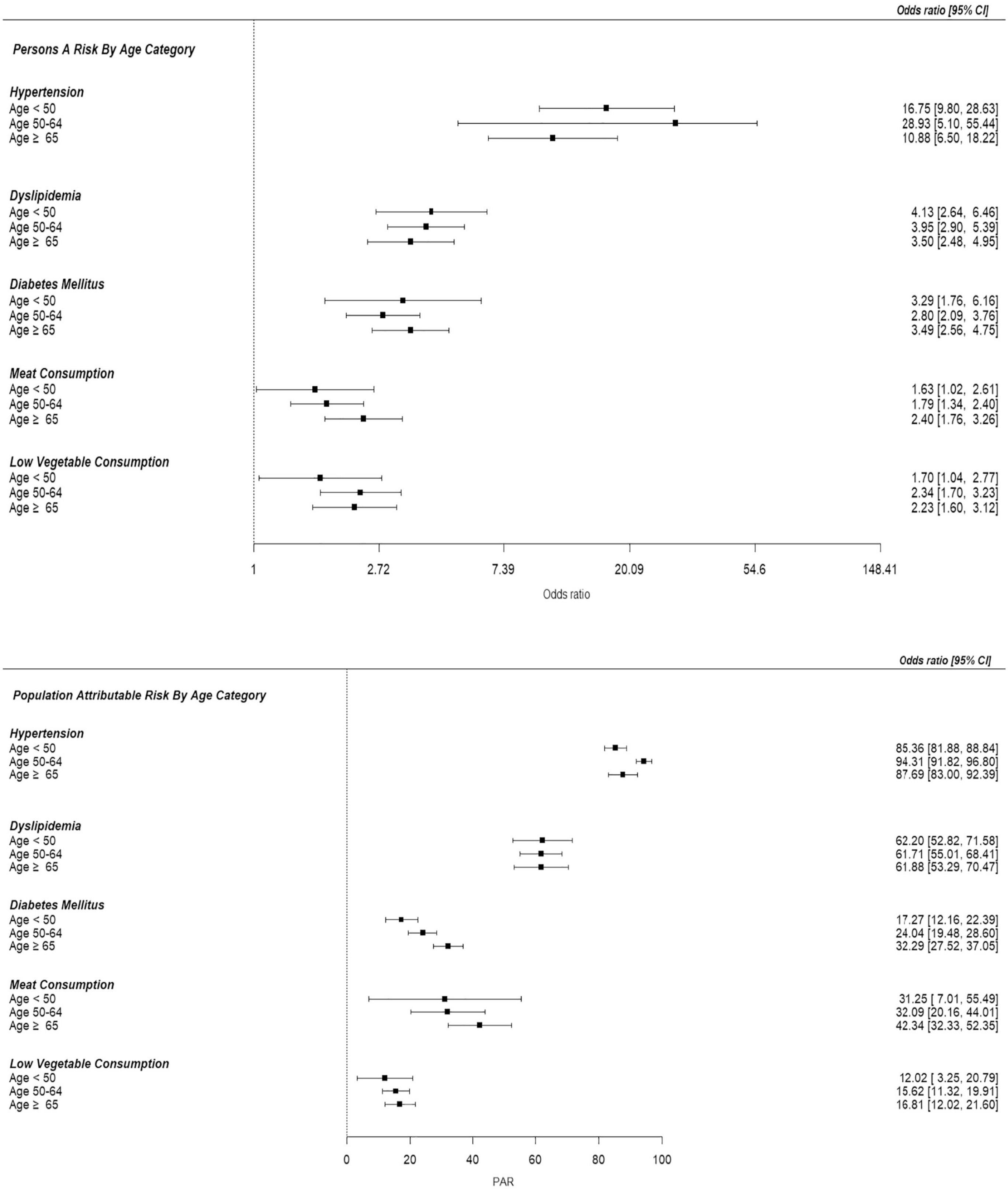

Fig. 3. Forest plot showing odds ratio (A) and population attributable risk (B) of the five dominant factors associated with stroke occurrence across the age strata.

However, routine screening for CVD risk stratification is seldom performed in clinics not to mention at the community level. Indeed, we found overall that the frequency of use of cardiovascular medications such as antiplatelets, statins and anticoagulants prior to the onset of stroke symptoms was low in this study. Hence, the low rates of utilization of anticoagulants and antiplatelets for instance meant that the contribution of these medications to the occurrence of intracerebral bleeds in our population was insignificant. We have previously reported on the low prescription of cardiovascular prevention medications among high CVD risk individuals in Ghana [21–24]. Individuals identified with

CVD risk could have risk mitigated using the cardiovascular polypills [25–27]. There are also preliminary data to suggest that resistant forms of hypertension may be commoner among Africans [28–30] requiring combinations of antihypertensive drug classes for control.

4.2. Limitations

We sought in this case-control study to assess associations and quantify effect sizes (population attributable risks and ORs) of risk factors but not to establish causality of these risk factors for stroke. Subjects with alterations in consciousness or dysphasia had their lifestyle and behavioral history assessed from valid proxies. Our previous reports and analysis suggest that the associations observed were in the same direction as those assessed directly [13,31]. An important strength of our study is the utilization of active community engagement activities before, during and after recruitment of stroke cases and controls to mitigate presentation bias to enhance the generalizability of our findings.

4.3. Conclusion

Lifestyle and pharmacological interventions aimed at detecting and addressing hypertension, dyslipidemia and diabetes mellitus allied with healthy dietary practices may form a foundation for stroke prevention in Africa. Achieving the WHO and Sustainable Development Goals (SDG) of reducing premature deaths from NCDs by 2030 would require a strong political commitment of African leaders [32,33]. The development of public health policy for stroke prevention must occur in tandem with implementation science research aimed at developing and testing multi-modal preventative interventions that transcends and surmounts the multitude of socio-cultural impediments of stroke prevention on the continent. The African Stroke Organization (ASO) will champion many of these initiatives to curtail stroke among Africans [34].

Conflicts

None to declare.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jns.2021.117573.

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