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Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Owolabi MO, Sarfo F, Akinyemi R, et al. Dominant modifiable risk factors for stroke in Ghana and Nigeria (SIREN): a case-control study. *Lancet Glob Health* 2018; published online S2214-109X(18)30002-0. http://dx.doi.org/10.1016/Feb 26.

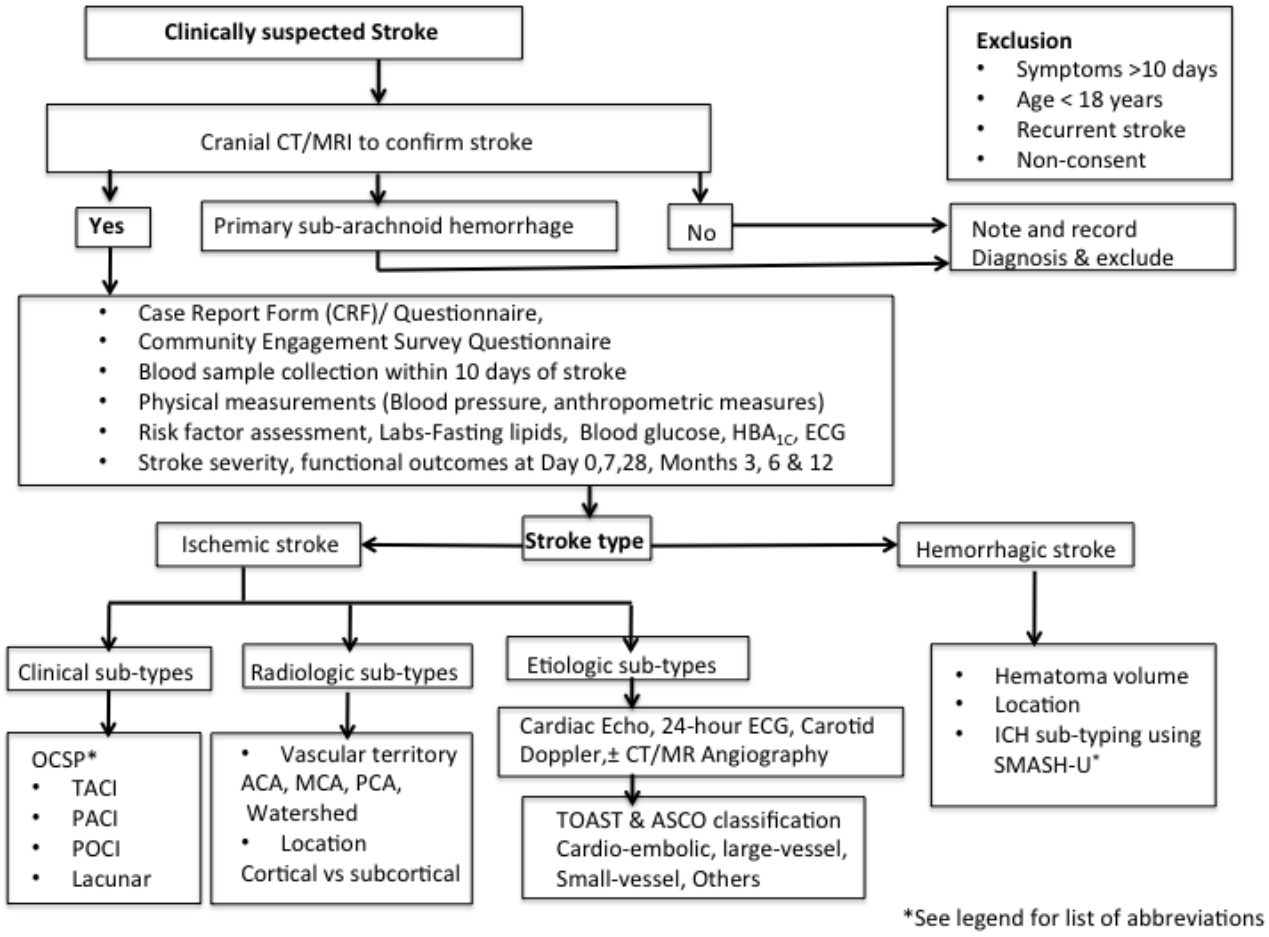
SUPPLEMENTARY MATERIAL

Table S1: Participating Study Sites in SIREN

Sites	Number of Case-control pairs (%)
1. Korle-Bu Teaching Hospital, Accra, Southern Ghana	483 (22.8)
2. Komfo Anokye Teaching Hospital, Kumasi, Middle Ghana	433 (20.4)
3. University College Hospital, Ibadan, South Western Nigeria	334 (15.8)
4. Blossom Medical Center, Ibadan, South Western Nigeria	16 (0.8)
5. Federal Medical Center, Abeokuta, Southern Nigeria	143 (6.8)
6. Sacred Heart Hospital, Abeokuta, Southern Nigeria	75 (3.5)
7. Ahmadu Bello University Teaching hospital, Zaria, Northern Nigeria	181 (8.5)
8. Aminu Kano Teaching Hospital, Kano, Northern Nigeria	144 (6.8)
9. Obafemi Awolowo University Teaching Hospital, Southern Nigeria	122 (5.8)
10. University of Ilorin Teaching Hospital, Southern Nigeria	100 (4.7)
11. LadokeAkintola University of Technology Hospital, Southern Nigeria	2 (0.1)
12. Jos University Teaching Hospital, Northern Nigeria	38 (1.8)
13. Delta State University Teaching Hospital, Southern Nigeria	3 (0.1)
14. Federal Teaching Hospital Ido-EKiti, Southern Nigeria	16 (0.8)
15. Federal Medical Centre (FMC), Owo, Southern Nigeria	28 (1.3)
Total	**2118 (100.0)**

Table S2: Exclusion criteria for cases

1	Patients unable to communicate because of severe stroke, aphasia, or dementia and without a valid surrogate respondent (spouse or first degree relative who has lived with patient within the last year)
2	Extra-axial hemorrhage, tumor or brain abscess
3	Subarachnoid haemorrhage
4	Current hospitalization for coronary heart disease
5	Unable to provide consent and no surrogate available
6	A known previous history of stroke.
7	Age <18 years



Legend: ACA=Anterior Cerebral Artery; MCA= Middle Cerebral Artery; ASCO= Atherosclerosis, Small vessel disease, Cardiac source, and Other; ECG=electrocardiography; OCSP= Oxfordshire Community Stroke Project criteria; PACI= Partial Anterior Circulation Infarct; PCA= Posterior Cerebral Artery; POCI= Posterior Circulation Infarct; TACI=Total Anterior Circulation Infarct; TOAST= Trial of Org 10172 in Acute Stroke Treatment

Figure S1. Algorithm for phenotypic characterization of stroke subjects [1]

Table S3. List of variables collected from subjects enrolled into SIREN study

Variable	Description
Psychosocial factors	Ethnicity, education, occupation, total monthly household income, stress, depression
Lifestyle factors	Tobacco use, exposure to environmental tobacco, alcohol use, dietary habits (for estimation of intake of fruits, vegetables, fried foods, meats, fish, added salt), physical activity.
Medical history	Hypertension, diabetes mellitus, smoking, hypercholesterolemia, atrial fibrillation, cardiovascular diseases, cancer, current medication use, other vascular disease, oral contraceptive use, hormone replacement, family history of cardiovascular diseases, migraine.
Physical measurements	Blood pressure height, weight, waist and hip circumferences according to Standard Operating procedures across all study sites.[1]
Neurological assessment	Clinical assessment for stroke severity using the modified NIHSS scale, Modified Rankin scale and stroke Levity scale.
Blood tests	Fasting lipid profile, Serum HbA1c, Fasting blood sugar.
Neuroimaging and cardiac evaluation	CT or MRI of brain (for all cases), ECG, Echocardiography (for all cases of suspected cardioembolic stroke), Carotid Doppler USS (planned for all cases of ischemic stroke, anterior circulation) were done at all sites following SOPs.
Stroke subtype	Based on clinical, laboratory assessments, and neuroimaging (e.g. CT of brain), ACCESS tool with excellent reliability.[2,3]

Table S4. List of potential biases in the SIREN study and how they were approached

Biases	Steps taken to minimize
Selection and referral bias	Biases may result from exclusion of 1) patients admitted with rapidly fatal stroke; 2) patients with severe stroke necessitating intubation; 3) exclusion of patients with aphasia or severe dysarthria; 4) non-hospitalized patients, since stroke with minor deficits may be less likely to be admitted and rates of hospitalization may differ between countries and 5) other variations in care pathways, particularly if patients with certain subtypes of strokes are admitted by non-neurologic sub-specialists (e.g. ischemic stroke admitted under medical service and ICH admitted under surgical service). These potential biases were approached by: 1) maintaining a Log/Registry of all patients admitted to a hospital with acute stroke by screening all stroke admissions 3 times a week, 2) use of surrogate respondents (defined above) for patients unable to communicate because of severe stroke or aphasia. 3) Broadening patient recruitment to include patients admitted to hospital, seen in emergency room and ambulatory clinics. 4) Community engagement outreaches were conducted across sites periodically to sensitize members of the community and encourage stroke patients to present in SIREN hospitals.
Diagnostic investigation bias	We developed a diagnostic algorithm and conducted regular training workshops to ensure similar level of investigations across sites. All our study sites were tertiary centers. Each site has a team comprising of neurologists, cardiologists, neuro-sonologists, neuroradiologists, and laboratory scientists. We developed and patented the ACCESS instrument[2] which has excellent inter-rater reliability for stroke phenotyping. For primary stroke type, inter-rater agreement was 0.98 (95% confidence interval [CI], .94-1.00), while intra-rater agreement was 1.00 (95% CI, 1.00). For OCSP subtypes, inter-rater agreement was 0.97 (95% CI, .92-1.00) for the partial anterior circulation infarcts, 0.92 (95% CI, .76-1.00) for the total anterior circulation infarcts, and excellent for both lacunar infarcts and posterior circulation infarcts. Intra-rater agreement was .97 (.90-1.00), while inter-rater agreement was 0.93 (95% CI, 0.84-1.00) for TOAST subtypes. Inter-rater agreement ranged between 0.78 (cardio-embolic) and 0.91 (large artery atherosclerotic) for ASCO subtypes and was 0.80 (95% CI, .56-1.00) for SMASH-U subtypes.
Recall bias	*Recall Bias* may result when the presence or absence of a medical condition may influence patients' or caregiver's ability to recall events.

	Where possible, objective evidence of risk factors by physical or laboratory measurements were performed.
Social desirability	*Social Desirability bias* may result from cases or controls under-reporting adverse lifestyle behaviours compared to controls, or over-report advantageous behaviours. However, the case-control methodology has been found to be reliable for a number of risk factors.[4]
Interviewer bias	*Interviewer Bias* may result from knowledge of case or control status. This may influence the manner that questions are asked or indirectly influence interviewee response. To overcome this potential bias, interviewers were trained to obtain information in a standardized fashion.

Table S5: Unadjusted OR and 95% CI for the association between stroke status and all variables

Variable	Unadjusted OR	Unadjusted 95% CI OR Lower limit	Unadjusted 95%CI OR Upper Limit
Country, Ghana, %	0.75	0.43	1.32
Gender, Male, %			
Age, mean ± SD	1.31	1.27	1.35
Age >65years, %	2.34	1.60	3.42
Age >= 50, %	3.78	2.39	5.99
Type of Domicile:			
Rural, %			
Semi-Urban, %	2.31	1.83	2.92
Urban, %	2.28	1.84	2.83
Monthly Income >$100, %	1.74	1.53	1.99
Education, (some) %	1.35	1.12	1.63
Hypertension, %	20.15	14.72	27.57
Dyslipidemia, %	2.33	2.03	2.69
Diabetes, %	4.14	3.49	4.91
Cardiac Disease, %	2.48	1.95	3.16
HDL-Cholesterol, mmol/l, mean ± SD	0.99	0.98	0.99
HDL-Cholesterol ≤ 1.03mmol/l, %	1.62	1.40	1.88
LDL-Cholesterol, mmol/l, mean ± SD	1.00	1.00	1.00
LDL-Cholesterol ≥ 3.4mmol/l, %	1.06	0.93	1.22
LDL/HDL ratio, mean ± SD	1.16	1.11	1.22
LDL/HDL ratio >2.96, %	1.33	1.16	1.53
LDL/HDL ratio by tertiles:			
≤ 2.00, %			
2.01 - 2.96, %	1.26	1.07	1.48
≥ 2.97, %	1.50	1.28	1.76
Total Cholesterol, mmol/l, mean ± SD	1.00	1.00	1.00
Total Cholesterol ≥ 5.2mmol/l, %	1.18	1.03	1.35
Triglyceride, mmol/l, mean ± SD	1.01	1.00	1.01
Triglyceride ≥ 1.7mmol/l, %	2.20	1.86	2.59
Waist-to-hip Ratio, mean ± SD	60.25	24.41	148.76
Waist-to-hip Ratio raised, %	2.06	1.77	2.42
Waist-to-hip Ratio by tertiles:			
≤ .90, %			
.91 - .96, %	1.87	1.60	2.19
≥.97+, %	2.09	1.77	2.46
WHR**, Lowest vs highest tertile, %	2.07	1.68	2.55
WHR**, 1st vs 2nd+3rd tertile, %	1.97	1.71	2.26
BMI*** (kg/m2), mean ± SD	1.00	0.99	1.02
BMI*** >30kg/m2, %	0.93	0.78	1.11
Physical Activity (some activity), %	2.09	1.46	2.99
Tobacco use in past 12 months, %	2.60	1.64	4.12
Tobacco (any use), %	1.32	1.05	1.65
Alcohol (current user), %	1.35	1.13	1.61
Alcohol (any use), %	1.29	1.12	1.50
Alcohol use categories:			

Never Use, %			
Ever Low Use, %	1.36	1.09	1.69
Ever High Use, %	5.82	2.58	13.12
Stress, %	1.76	1.48	2.10
Cancer, %	2.75	0.88	8.64
Depression, %	1.25	0.98	1.60
Family history of CVD, %	1.81	1.57	2.08
Adding salt at table, %	1.53	1.19	1.96
Adding salt at table categories:			
Never/rarely, %			
Occasionally, %	2.00	1.67	2.40
Very often, %	1.72	1.33	2.22
Green vegetable consumption, %	2.04	1.73	2.42
Whole grains consumption, %	1.26	1.05	1.51
Legumes consumption, %	1.12	0.97	1.29
Fruit consumption, %	0.72	0.60	0.87
Sugar consumption or otherwise, %	0.82	0.71	0.94
Meat consumption or otherwise	1.34	1.13	1.59
Fish consumption or otherwise, %	1.10	0.85	1.42

Table S6: Unadjusted OR and 95% CI for the association between stroke status and all variables by stroke type

	Hemorrhagic Stroke			Ischemic Stroke		
Variables	**Unadjusted OR**	**Unadjusted 95%CI Lower limit**	**Unadjusted 95%CI Upper limit**	**Unadjusted OR**	**Unadjusted 95%CI Lower limit**	**Unadjusted 95%CI Upper limit**
Country, Ghana, %	0.80	0.32	2.03	0.72	0.35	1.47
Gender, Male, %						
Age, mean ± SD	1.29	1.22	1.36	1.32	1.27	1.37
Age >65years, %	1.40	0.62	3.15	2.68	1.74	4.13
Age >= 50, %	6.20	2.41	15.94	3.11	1.83	5.29
Type of Domicile:						
Rural, %						
Semi-Urban, %	2.22	1.45	3.40	2.33	1.76	3.09
Urban, %	2.02	1.36	3.00	2.41	1.86	3.12
Monthly Income >$100, %	1.59	1.27	1.99	1.83	1.55	2.15
Education, (some) %	1.44	1.00	2.07	1.32	1.06	1.64
Hypertension, %	63.20	26.12	152.89	14.17	10.10	19.86
Dyslipidemia, %	1.76	1.39	2.23	2.71	2.27	3.24
Diabetes, %	2.98	2.20	4.04	4.74	3.85	5.83
Cardiac Disease, %	1.62	0.99	2.63	2.82	2.13	3.73
HDL-Cholesterol, mmol/l, mean ± SD	1.00	1.00	1.01	0.98	0.97	0.98
HDL-Cholesterol ≤ 1.03mmol/l, %	1.03	0.80	1.32	2.01	1.68	2.40
LDL-Cholesterol, mmol/l, mean ± SD	1.00	1.00	1.00	1.00	1.00	1.00
LDL-Cholesterol ≥ 3.4mmol/l, %	1.06	0.85	1.34	1.07	0.90	1.26
LDL/HDL ratio, mean ± SD	1.08	1.00	1.17	1.21	1.14	1.28
LDL/HDL ratio >2.96, %	1.02	0.81	1.29	1.52	1.29	1.80
LDL/HDL ratio by tertiles:						
≤ 2.00, %						
2.01 - 2.96, %	1.09	0.82	1.44	1.35	1.11	1.66

≥ 2.97, %	1.07	0.81	1.41	1.78	1.46	2.17
Total Cholesterol, mmol/l, mean ± SD	1.00	1.00	1.00	1.00	1.00	1.00
Total Cholesterol ≥ 5.2mmol/l, %	1.30	1.02	1.64	1.13	0.96	1.33
Triglyceride, mmol/l, mean ± SD	1.01	1.00	1.01	1.01	1.00	1.01
Triglyceride ≥ 1.7mmol/l, %	2.03	1.50	2.75	2.27	1.86	2.77
Waist-to-hip Ratio, mean ± SD	320.79	58.29	1765.30	28.87	9.98	83.56
Waist-to-hip Ratio raised, %	2.49	1.93	3.21	1.83	1.50	2.24
Waist-to-hip Ratio by tertiles:						
≤ .90, %						
.91 - .96, %	2.10	1.62	2.72	1.74	1.42	2.12
≥.97+, %	2.58	1.93	3.47	1.87	1.52	2.29
WHR**, Lowest vs highest tertile, %	2.54	1.75	3.68	1.87	1.45	2.41
WHR**, 1st vs 2nd+3rd tertile, %	2.28	1.81	2.87	1.80	1.51	2.14
BMI*** (kg/m2), mean ± SD	0.98	0.96	1.00	1.02	1.00	1.03
BMI*** >30kg/m2, %	0.70	0.51	0.96	1.06	0.86	1.32
Physical Activity (some activity), %	2.42	1.23	4.74	1.97	1.29	3.01
Tobacco use in past 12 months, %	3.56	1.70	7.45	2.06	1.14	3.75
Tobacco (any use), %	1.80	1.19	2.72	1.14	0.87	1.50
Alcohol (current user), %	1.87	1.40	2.50	1.11	0.89	1.39
Alcohol (any use), %	1.64	1.27	2.11	1.14	0.95	1.37
Alcohol use categories:						
Never Use, %						
Ever Low Use, %	1.59	1.11	2.29	1.24	0.94	1.64
Ever High Use, %	22.87	3.03	172.43	3.17	1.25	8.02
Stress, %	1.53	1.15	2.04	1.91	1.54	2.38
Cancer, %	NA	NA	NA	2.25	0.69	7.31
Depression, %	1.30	0.84	1.99	1.23	0.91	1.66
Family history of CVD, %	1.64	1.29	2.08	1.90	1.59	2.26
Adding salt at table, %	1.62	1.08	2.44	1.48	1.08	2.02

Adding salt at table categories:						
Never/rarely, %						
Occasionally, %	2.28	1.62	3.20	1.89	1.53	2.35
Very often, %	1.82	1.20	2.76	1.66	1.21	2.29
Green vegetable consumption, %	2.33	1.71	3.17	1.93	1.58	2.36
Whole grains consumption, %	1.06	0.78	1.45	1.37	1.10	1.71
Legumes consumption, %	1.07	0.84	1.36	1.14	0.96	1.36
Fruit consumption, %	0.60	0.43	0.84	0.78	0.62	0.98
Sugar consumption or otherwise, %	0.78	0.62	0.99	0.84	0.70	0.99
Meat consumption or otherwise	1.31	0.97	1.77	1.36	1.10	1.67
Fish consumption or otherwise, %	1.39	0.87	2.20	0.99	0.72	1.35

Table S7. Stroke Primary types and subtypes

Stroke type	Frequency	Percentage
Ischemic	1407	66.4
Haemorrhagic	682	32.2
Ischemic with haemorrhagic transformation	23	1.1
Coexisting distinct Ischemic and Haemorrhagic	6	0.3
Total	**2118**	**100.0**
Ischemic Stroke subtypes and classifications		
OCSP classification*		
Partial anterior circulation infarction	547	46.0
Total anterior circulation infarction	199	16.7
Lacunar infarction	505	42.5
Posterior circulation infarction	201	16.9
TOAST classification (presumed dominant ischemic subtype)#		
Large artery-atherosclerosis, embolus/thrombosis	411	33.8
Cardioembolism, high-risk/medium-risk	102	8.4
Small-vessel occlusion, lacune	455	37.4
Other determined etiology (Dissection, Vasculitis, CVST, Others)	1	0.1
Undetermined etiology (Two or more causes identified, negative evaluation, Incomplete evaluation)	247	20.3
Sub-total	**1,216**	**100.0**
ASCO classification#*		
Atherosclerotic	324	36.9
Small vessel	519	59.1
Cardioembolic	159	18.1
Others	27	3.1
Hemorrhagic stroke subtypes#*		
Structural	40	7.2
Medication related	6	1.1
Amyloid angiopathy	12	2.2
Systemic disease	10	1.8
Hypertension	520	93.9
Undetermined	10	1.8

CVST= Central venous sinus thrombosis

** An individual subject may have more than one coexisting subtype

Information not available for all subjects

Table S8 – Comparison of characteristics of Stroke primary type (Case-case Analysis).

Variable	Total Sample	Stroke Primary Type		*p*-value
		Haemorrhagic (n=682)	Ischemic (n=1,430)	
Gender, Male, %	56.3	62.8	53.3	<0.001
Age, mean ± SD	58.99±13.82	53.45±12.76	61.60±13.51	<0.001
Age >65years, %	31.8	16.1	39.3	<0.001
Monthly Income >$100, %	56.7	57.0	56.5	0.837
Education, (some) %	83.7	89.1	81.1	<0.001
Hypertension, %	95.1	97.6	93.9	<0.001
Dyslipidemia, %	78.4	74.5	80.2	0.003
Diabetes, %	37.9	27.3	43.0	<0.001
Cardiac Disease, %	11.8	6.7	14.3	<0.001
HDL-Cholesterol, mmol/l, mean ± SD	1.27±0.49	1.39±0.53	1.21±0.47	<0.001
HDL-Cholesterol ≤ 1.03mmol/l, %	33.7	24.2	38.2	<0.001
LDL-Cholesterol, mmol/l, mean ± SD	3.25±1.33	3.36±1.34	3.20±1.32	0.011
LDL-Cholesterol ≥ 3.4mmol/l, %	42.0	43.7	41.3	0.308
LDL/HDL ratio, mean ± SD	2.95±1.84	2.80±1.98	3.02±1.76	0.014
LDL/HDL ratio >2.96, %	38.7	34.0	40.9	0.003
LDL/HDL ratio by tertiles:				
≤ 2.00, %	30.1	34.0	28.2	0.005
2.01 - 2.96, %	31.2	32.0	30.9	
≥ 2.97, %	38.7	34.0	40.9	
Total Cholesterol, mmol/l, mean ± SD	5.11±1.51	5.25±1.48	5.04±1.52	0.003
Total Cholesterol ≥ 5.2mmol/l, %	45.6	48.4	44.3	0.082
Triglyceride, mmol/l, mean ± SD	1.47±0.99	1.041±098	1.50±0.98	0.040
Triglyceride ≥ 1.7mmol/l, %	26.4	22.9	28.0	0.013
Waist-to-hip Ratio, mean ± SD	0.94±0.08	0.93±0.07	0.94±0.08	0.023
Waist-to-hip Ratio raised, %	81.4	79.1	82.6	0.067
Waist-to-hip Ratio by tertiles:				
≤ .90, %	28.4	30.9	27.2	0.069
.91 - .96, %	37.0	37.9	36.6	
≥.97+, %	34.5	31.2	36.2	
WHR**, Lowest vs highest tertile, %	54.8	50.2	57.1	0.024
WHR**, 1st vs 2nd+3rd tertile, %	71.8	69.1	72.8	0.087
BMI*** (kg/m^2), mean ± SD	26.55±5.08	26.30±	26.66±5.08	0.201
BMI*** >30kg/m^2, %	21.3	19.0	22.4	0.133
Physical Activity (some activity), %	95.2	95.5	95.1	0.647
Tobacco use in past 12 months, %	3.5	5.1	2.7	0.005

Tobacco (any use), %	9.8	10.4	9.5	0.51
Alcohol (current user), %	19.2	26.6	15.6	<0.001
Alcohol (any use), %	36.5	43.5	33.2	<0.001
Alcohol use categories:				
Never Use, %	75.4	67.6	79.2	<0.001
Ever Low Use, %	21.6	27.8	18.7	
Ever High Use, %	2.9	4.6	2.1	
Stress, %	23.4	24.4	23.0	0.495
Cancer, %	0.5	0.3	0.7	0.315
Depression, %	9.1	9.1	9.0	0.976
Family history of CVD, %	40.8	42.0	40.2	0.437
Adding salt at table, %	8.4	10.1	7.6	0.059
Adding salt at table categories:				
Never/rarely, %	70.5	71.6	68.2	0.306
Occasionally, %	21.2	20.4	22.9	
Very often, %	8.3	8.1	8.9	
Green vegetable consumption, %	70.9	70.0	71.3	0.533
Whole grains consumption, %	86.0	85.4	86.2	0.643
Legumes consumption, %	66.9	68.4	66.1	0.299
Fruit consumption, %	82.9	81.9	933	0.435
Sugar consumption or otherwise, %	31.4	34.6	29.8	0.032
Meat consumption or otherwise	83.5	85.2	82.6	0.141
Fish consumption or otherwise, %	93.4	93.8	93.1	0.571

Values are means ± standard deviation or percentages.
Values of polytomous variables may not sum to 100% due to rounding, p-values reported for Independent t-test, Chi-square χ2.
***WHR= Waist-to-Hip Ratio*
****BMI= Body Mass Index*
**MRI/CT brain scan was available for 2,118 (100%), lipid profile for 2,113 (99.8%), HbA1c for 1,717 (81.1%), and fasting blood glucose for 1,530 (72%) cases; while 1,597 (75.4%) cases had ECG, 916 (43.2%) had transthoracic echocardiography, and 974 (46.0%) had carotid Doppler studies. Study questionnaires were completed by 1,621 (76.2%) proxy respondents, 414 (19.6%) patients and by both 77 (3.6%).*
#1758 (83.2%) controls were recruited from communities (catchment population of the stroke cases) while 328 (16.8%) were hospital-based controls from the same hospitals.

Table S9. Measures of stroke severity

Stroke Levity Score[5] at baseline	**Frequency**	**Percentage**
Mild (11-15)	310	16.3
Moderate (6-10)	627	33.0
Severe (0-5)	965	50.7
Total	**1902**	
Modified National Institute of Health Stroke Severity score[6] at baseline		
Mild (1-5)	275	14.5
Mild to Moderately severe (6-14)	745	39.2
Severe (15-25)	584	30.8
Very Severe (>25)	295	15.5
Total	**1899**	
Modified Rankin Scale[7] at baseline		
0 - No Symptoms at all	24	1.2
1 - No significant disability despite symptoms	80	4.1
2- Slight disability	115	5.9
3 - Moderate disability	130	6.7
4 - Moderately severe disability	902	46.6
5 - Severe disability	677	35.0
6 - Dead	9	0.5
Total	**1937**	

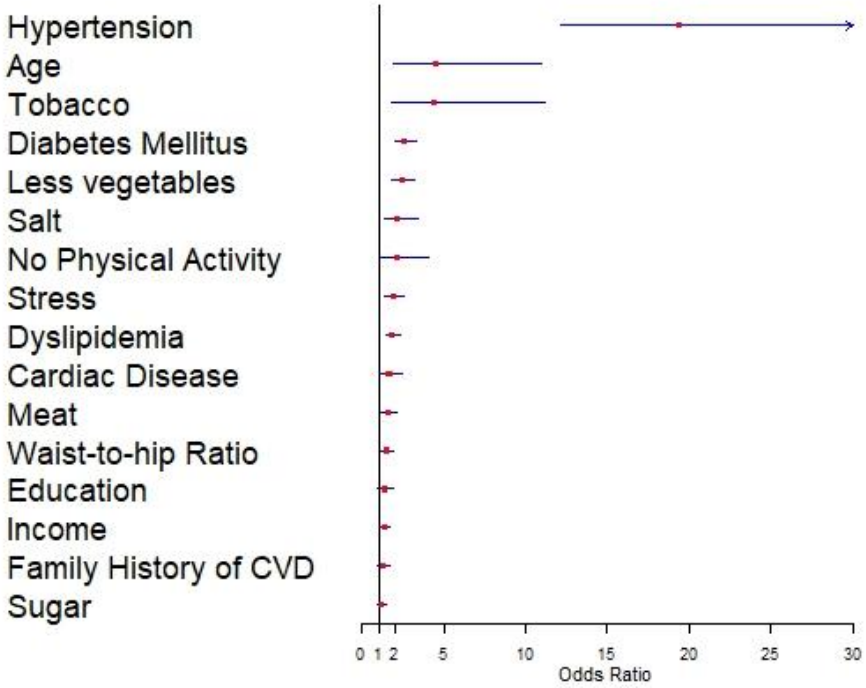


Figure S2A

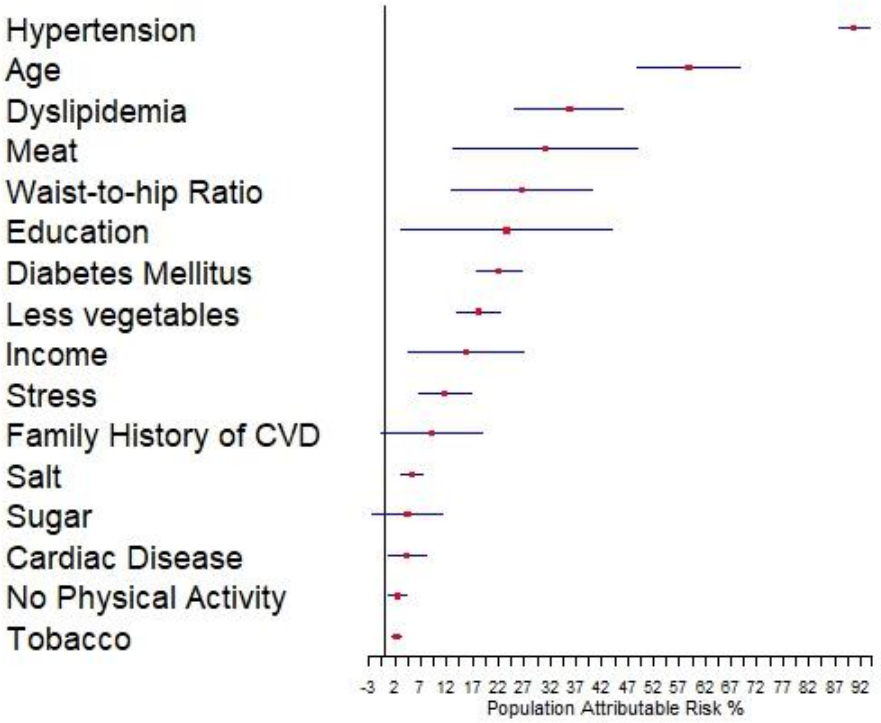


Figure S2B

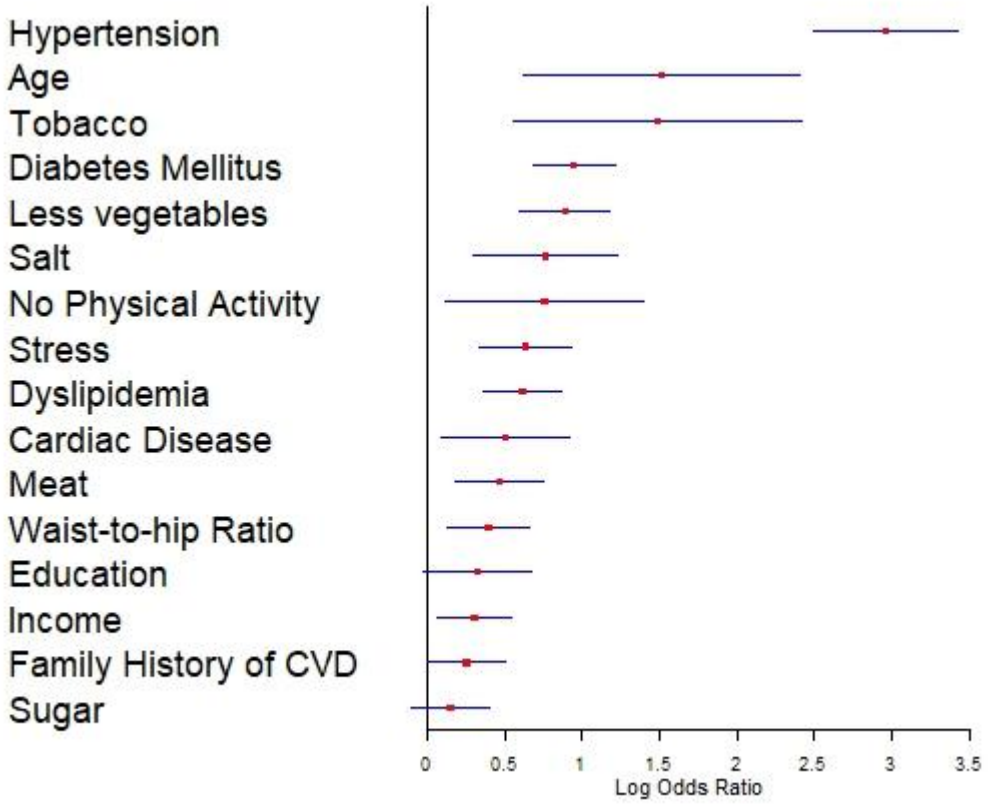


Figure S2C

Figure S2. Risk Factors for stroke among Africans. Risk factors are depicted as Forest Plots showing Odds Ratio (OR) (Figure S2A) and Population Attributable Risk (PAR) (Figure S2B).

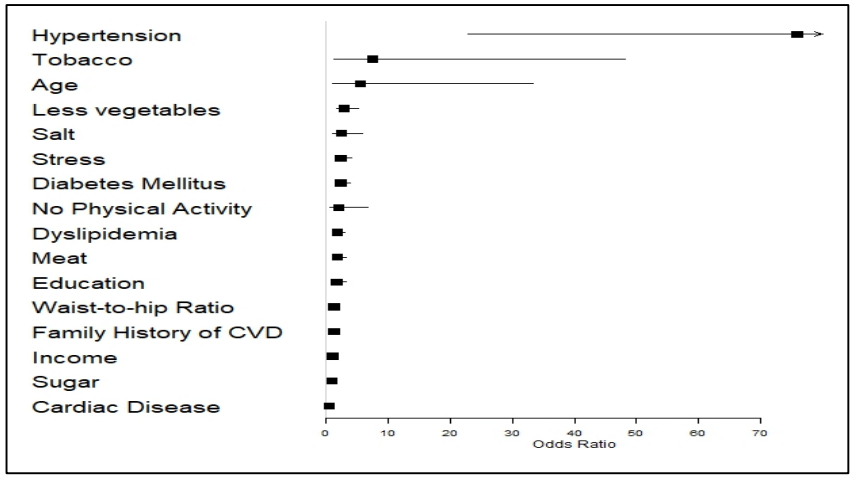


Figure S3A (Hemorrhagic Stroke)

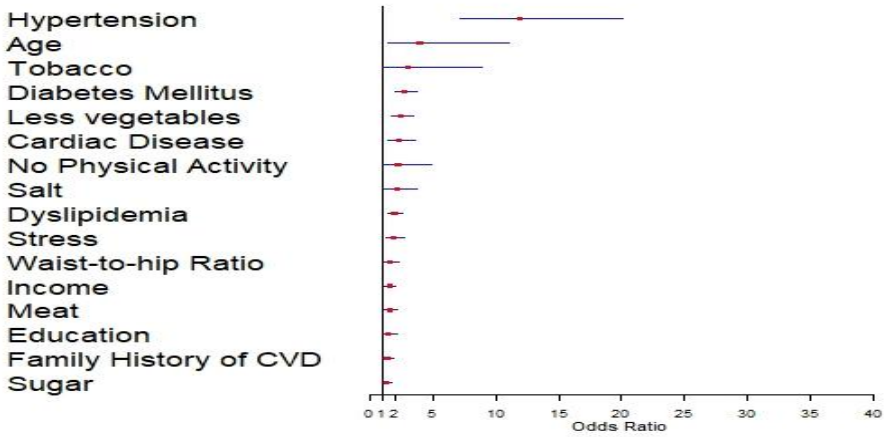


Figure S3B (Ischemic Stroke)

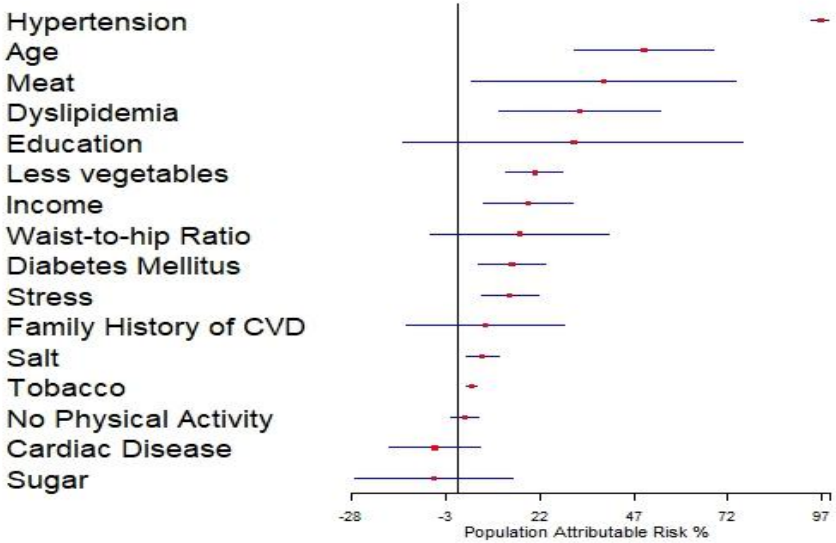


Figure S3C (Hemorrhagic Stroke)

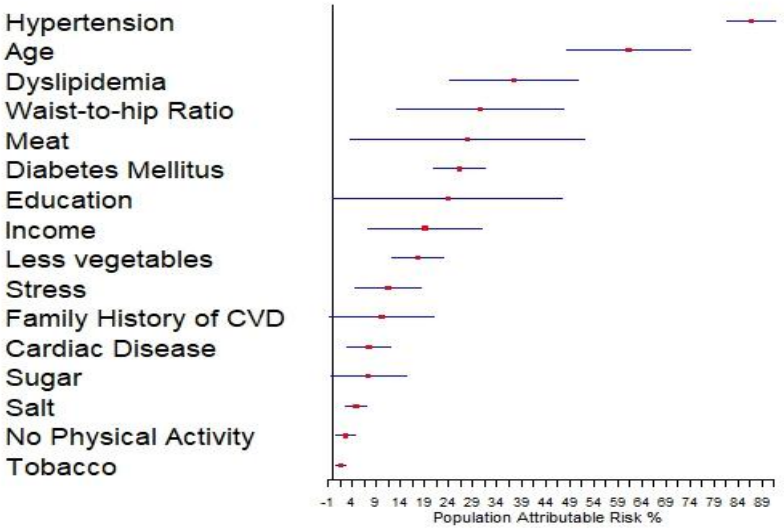


Figure S3D (Ischemic Stroke)

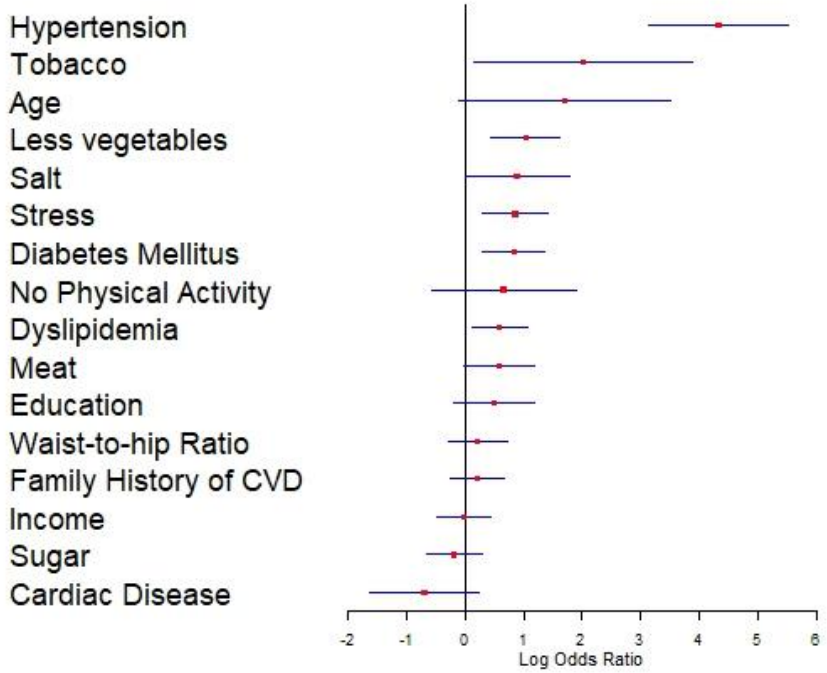


Figure S3E (Hemorrhagic Stroke)

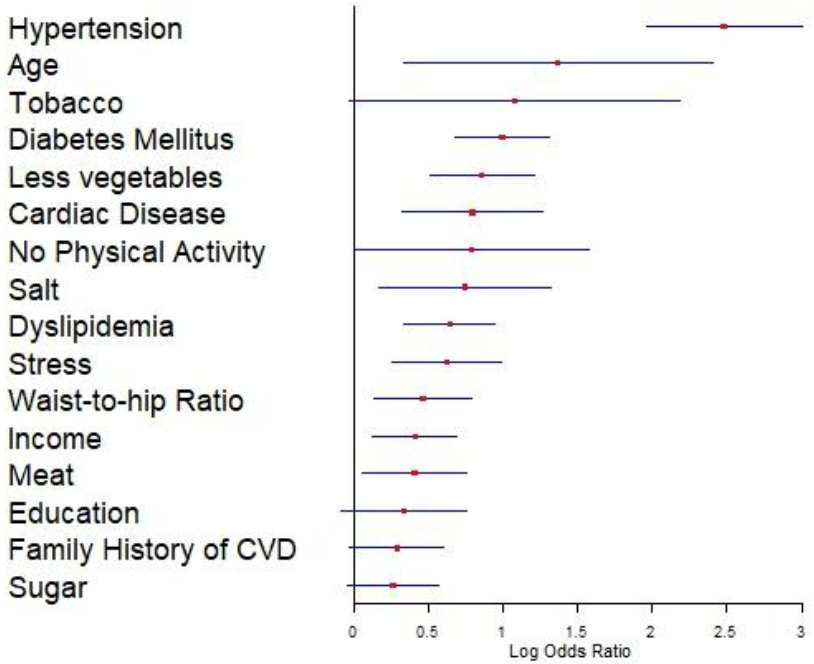


Figure S3F (Ischemic Stroke)

Figure S3. Risk Factors for ischemic and hemorrhagic stroke types among Africans. Risk factors are depicted as Forest Plots showing Odds Ratio (OR) : Figures 3A (hemorrhagic) and 3B (ischemic strokes); Population Attributable Risk (PAR)) :Figures 3C (hemorrhagic) and 3D (ischemic strokes); and Log odds ratio : Figures 3E (hemorrhagic) and 3F (ischemic strokes).

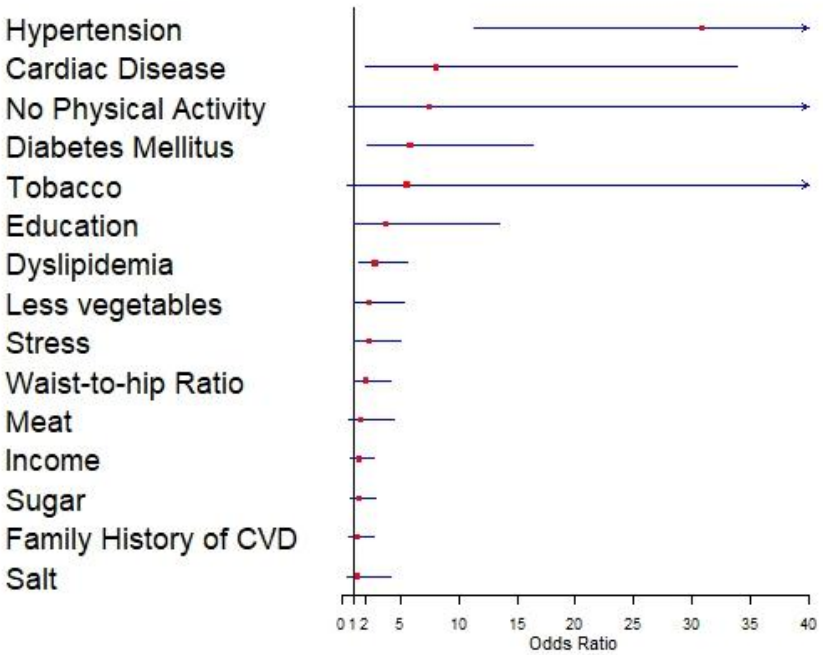


Figure S4A (Age < 50 years)

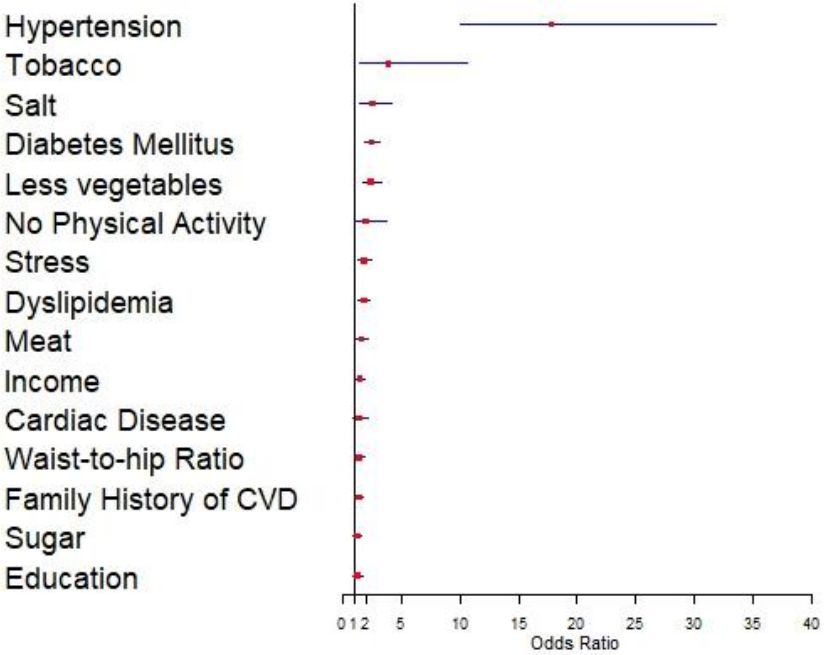


Figure S4B (Age ≥ 50years)

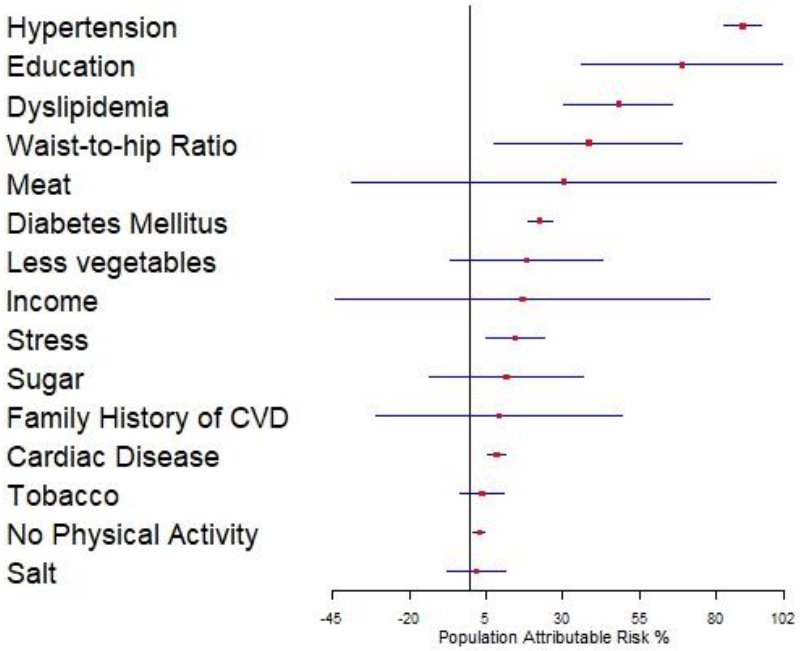


Figure S4C (Age < 50 years)

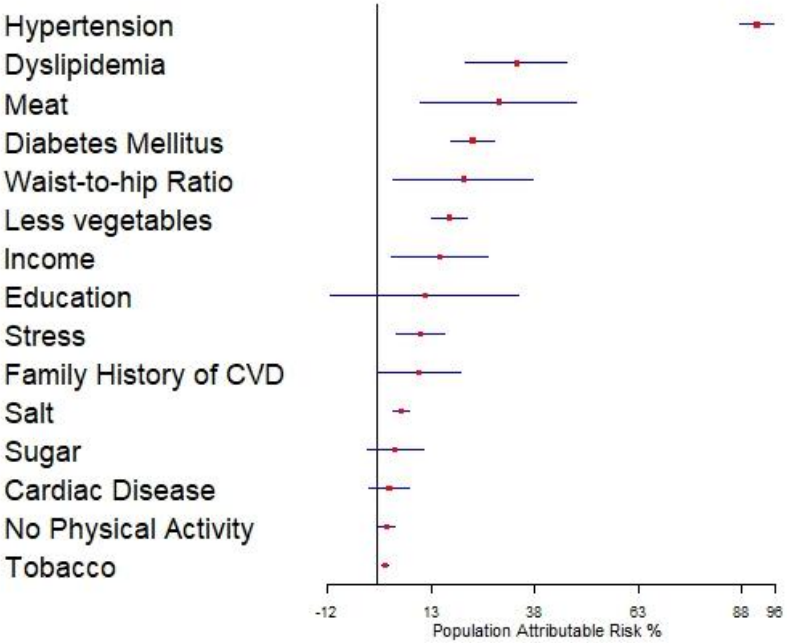


Figure S4D (Age ≥50years)

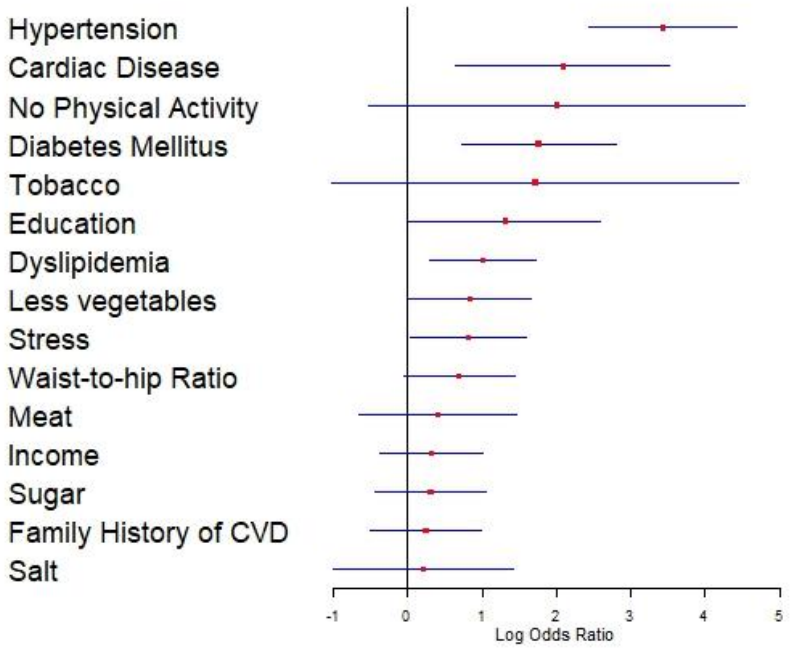


Figure S4E (Age < 50 years)

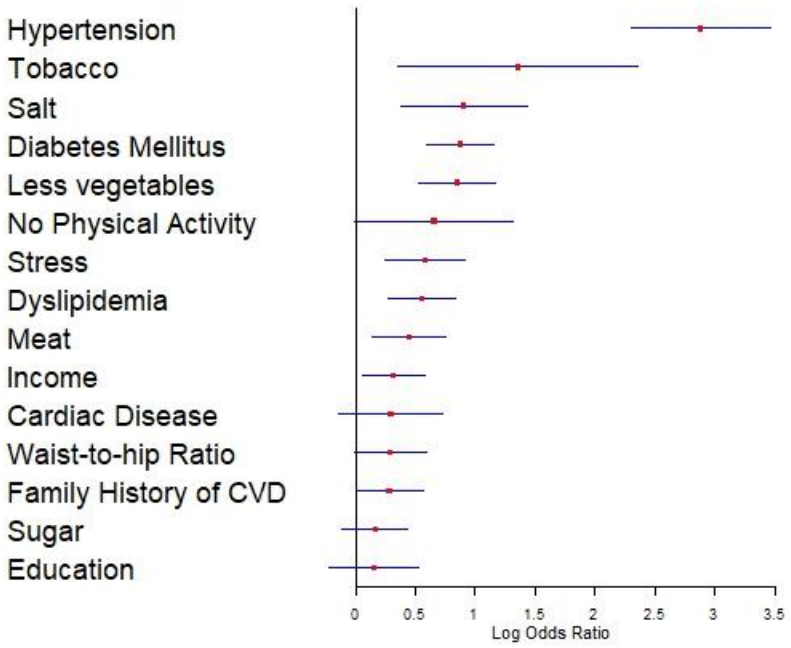


Figure S4F (Age ≥50years)

Figure S4. Risk Factors for stroke among Africans aged <50 years and ≥50years. Risk factors are depicted as Forest Plots showing Odds Ratio (OR) (Figures S4A for age <50 years and S4B for ≥50years); Population Attributable Risk (PAR) (Figures S4C for age <50 years and S4D for ≥50years) and Log Odds Ratio (OR) (Figures S4E for age <50 years and S4F for ≥50years) .

Table S10. Adjusted, Conditional Logistic Regression, by Country for stroke and stroke type

Predictor	Nigeria			Ghana		
	All Stroke OR (95% CI)	Hemorrhagic OR (95% CI)	Ischemic OR (95% CI)	All Stroke OR (95% CI)	Hemorrhagic OR (95% CI)	Ischemic OR (95% CI)
Age ≥ 50	5.02 (1.42-17.78)	3.08 (0.19-50.68)	6.04 (1.41-25.80)	3.76 (0.97-14.74)	7.87 (0.50-122.74)	2.58 (0.48-13.84)
Monthly income	2.26 (1.60-3.20)	2.48 (1.10-5.58)	2.16 (1.46-3.21)	0.81 (0.57-1.15)	0.47 (0.23-0.93)	1.01 (0.65-1.56)
Education	1.41 (0.88-2.27)	1.75 (0.59-5.23)	1.35 (0.78-2.35)	0.92 (0.50-1.67)	0.79 (0.24-2.57)	1.00 (0.47-2.13)
Hypertension	20.55 (10.45-40.40)	88.01 (10.65-727.43)	14.78(7.05-30.97)	19.96 (9.89-40.26)	105.92(18.36-611.06)	10.66 (4.74-23.97)
Dyslipidemia	1.76 (1.23-2.50)	1.26 (0.60-2.67)	1.98 (1.30-3.02)	1.95 (1.31-2.89)	2.13 (1.02-4.45)	1.79 (1.09-2.95)
Diabetes mellitus	2.58 (1.74-3.81)	2.45 (0.92-6.49)	2.59 (1.67-4.01)	2.49 (1.68-3.69)	2.26 (1.10-4.65)	2.70 (1.63-4.48)
Cardiac disease	1.24 (0.67-2.28)	**	1.50 (0.76-2.98)	2.07 (1.16-3.71)	**	2.98 (1.47-6.04)
Physical Activity	1.29 (0.19-8.60)	6.50 (0.03-1313.0)	0.98 (0.12-8.07)	2.22 (1.10-4.46)	1.29 (0.33-5.09)	3.04 (1.22-7.61)
Increased WHR	2.31 (1.54-3.46)	1.79 (0.79-4.04)	2.54 (1.55-4.16)	0.98 (0.66-1.47)	0.81 (0.37-1.80)	0.97 (0.59-1.60)
Stress	3.07 (1.90-4.96)	2.24 (0.76-6.61)	3.31 (1.88-5.83)	1.29 (0.87-1.94)	2.66 (1.21-5.85)	1.01 (0.60-1.71)
Salt	1.84 (0.93-3.66)	1.30 (0.30-5.57)	2.02 (0.90-4.54)	2.58 (1.28-5.18)	2.74 (0.80-9.32)	3.00 (1.17-7.69)
Meat	1.96 (1.20-3.19)	5.20 (1.07-25.33)	1.67 (0.99-2.82)	1.42 (0.97-2.09)	1.72 (0.81-3.61)	1.32 (0.82-2.14)
Green Vegetable	2.46 (1.64-3.67)	3.36 (1.34-8.45)	2.28 (1.45-3.58)	2.61 (1.61-4.25)	2.24 (0.90-5.56)	2.92 (1.57-5.43)
Sugar	1.41 (1.00-2.01)	1.45 (0.73-2.88)	1.38 (0.90-2.11)	1.06 (0.72-1.56)	0.49 (0.21-1.16)	1.38 (0.85-2.22)
Tobacco	2.74 (0.63-11.96)	1.50 (0.12-18.36)	4.12 (0.66-25.75)	5.40 (1.62-18.00)	10.57(0.94-118.92)	2.59 (0.57-11.66)
Family History of CVD	1.06 (0.69-1.63)	0.84 (0.35-5.57)	1.12 (0.67-1.88)	2.58 (1.28-5.18)	2.12 (1.04-4.32)	1.75 (1.13-2.70)

WHR: waist hip ratio ** Cardiac disease was associated with unstable estimates.

Table S11: Association of Hypertension with Stroke

Self-reported history of ***hypertension or blood pressure ≥ 140mmHg, using***	ALL STROKE		ISCHEMIC STROKE	HEMORRHAGIC STROKE
	OR (95%CI)	**Cumulative PAR (95%) for stroke based on definition of hypertension**	**OR (95%CI)**	**OR (95%CI)**
Using different definitions of hypertension in cases with application of correction factor to Systolic BP after stroke based on OXVASC study[8]				
Mean of 3 blood pressure measurements ***≥ 140mmHg*** (time of admission and morning after admission	5.28 (3.98 - 7.01)	95.7 (93.9 – 97.4)	4.97 (3.48 – 7.10)	6.54 (3.96 - 10.82)
Blood pressure at time of admission ***≥ 140mmHg***	5.79 (4.32 - 7.76)	95.8 (93.9-97.3)	5.05 (3.52 - 7.25)	8.00 (4.69 - 13.64)
Blood pressure at morning after admission ***≥ 140mmHg***	4.60 (3.51 - 6.03)	95.2 (93.1 – 97.0)	4.36 (3.09 - 6.14)	5.45 (3.40 - 8.75)
Blood pressure at time of interview ***≥ 140mmHg*** or new introduction of antihypertensive medications after admission	17.87 (11.49 - 27.78)	98.1 (97.3-99.0)	11.66 (7.16 - 18.97)	65.47 (19.99 - 214.48)
Using different definitions of hypertension in cases without application of correction factors to Systolic BP after stroke based on OXVASC Study[8]				
Mean of 3 blood pressure measurements ***≥ 140mmHg*** (time of admission and morning after admission	8.42 (6.06 - 11.69)	96.7 (95.1 – 98.0)	6.73 (4.52 - 10.02)	15.51 (8.09 - 29.73)
Blood pressure at time of admission ***≥ 140mmHg***	8.09 (5.85 - 11.17)	96.6 (95.2 - 97.9)	6.30 (4.26 - 9.30)	15.46 (8.08 - 29.58)
Blood pressure at morning after admission ***≥ 140mmHg***	5.58 (4.19 - 7.42)	95.7 (94.0 – 97.2)	4.82 (3.38 - 6.88)	7.56 (4.52 - 12.63)
Blood pressure at time of interview ***≥ 140mmHg*** or new introduction of antihypertensive medications after admission	20.62 (12.90 - 32.94)	98.2 (97.2 – 99.0)	13.44 (8.00 - 22.58)	75.11 (22.32 - 252.77)

Adjusted OR includes all covariate from main adjusted model (Table 2) : SIREN Hypertension definition is replaced by each of 4 definitions provided. BP were corrected to prestroke levels using correction factors from the OXVASC study.

Table S12. Adjusted, Conditional Logistic Regression, by Control Source

Predictor	Other (n = 328)				Community (n = 1,758)			
		95% CI OR				95% CI OR		
	Odds ratio	Lower	Upper	*p*-value	Odds ratio	Lower	Upper	*p*-value
Age ≥50	2.04	0.20	20.62	0.547	4.16	1.688	10.24	0.002
Monthly income	0.84	0.45	1.54	0.563	1.49	1.161	1.92	0.002
Education	1.77	0.68	4.59	0.244	1.38	0.968	1.97	0.075
Hypertension	20.62	5.77	73.63	<0.0001	19.61	12.299	31.27	<0.0001
Diabetes Mellitus	2.15	1.11	4.18	0.023	2.81	2.116	3.73	<0.0001
Physical Inactivity	0.35	0.12	1.07	0.065	0.54	0.265	1.08	0.082
Alcohol	1.16	0.59	2.25	0.669	1.07	0.797	1.44	0.655
Stress	0.83	0.40	1.71	0.605	2.32	1.650	3.27	<0.0001
Depression	0.38	0.14	1.07	0.067	0.70	0.436	1.13	0.141
Salt	2.20	0.68	7.12	0.187	1.87	1.126	3.11	0.016
Meat	1.98	1.01	3.87	0.045	1.73	1.248	2.39	0.001
Green Vegetable	0.88	0.37	2.09	0.773	0.40	0.296	0.55	<0.0001
Tobacco	6.14	0.83	45.74	0.076	2.72	1.080	6.87	0.034
Family History of CVD	1.37	0.74	2.53	0.321	1.39	1.054	1.84	0.020
Sugar	1.57	0.74	3.33	0.238	1.08	0.837	1.40	0.546
Cardiac Disease	2.14	0.78	5.92	0.141	1.78	1.128	2.81	0.013

Table S13. Adjusted, Conditional Logistic Regression, by Case Respondent Type

Predictor	Proxy (n = 1,621)				Self (n = 414)			
	95% CI OR				95% CI OR			
	OR	Lower	Upper	*p*-value	OR	Lower	Upper	*p*-value
Age ≥ 50	4.05	1.56	10.48	0.004	5.70	0.80	40.71	0.083
Monthly income	1.46	1.12	1.91	0.005	1.17	0.69	2.00	0.562
Education	1.56	1.07	2.28	0.021	1.31	0.57	3.01	0.523
Hypertension	24.30	14.36	41.12	<0.0001	26.56	8.48	83.18	<0.0001
Diabetes Mellitus	3.49	2.58	4.73	<0.0001	0.99	0.55	1.76	0.963
Physical Activity	0.48	0.26	0.89	0.020	1.99	0.28	14.27	0.494
Alcohol	1.02	0.75	1.39	0.888	1.20	0.65	2.22	0.563
Stress	1.80	1.27	2.56	0.001	2.57	1.24	5.31	0.011
Depression	0.67	0.42	1.09	0.109	0.53	0.20	1.43	0.211
Salt	2.26	1.30	3.95	0.004	1.03	0.39	2.72	0.951
Meat	1.80	1.30	2.49	<0.0001	1.45	0.71	2.96	0.307
Green Vegetable	0.40	0.29	0.56	<0.0001	0.49	0.24	1.00	0.050
Tobacco	3.52	1.30	9.54	0.014	4.24	0.73	24.67	0.108
Family History of CVD	1.21	0.91	1.62	0.194	2.45	1.33	4.53	0.004
Sugar	1.17	0.89	1.54	0.264	0.95	0.53	1.72	0.864
Cardiac Disease	1.71	1.07	2.74	0.025	1.75	0.68	4.56	0.249

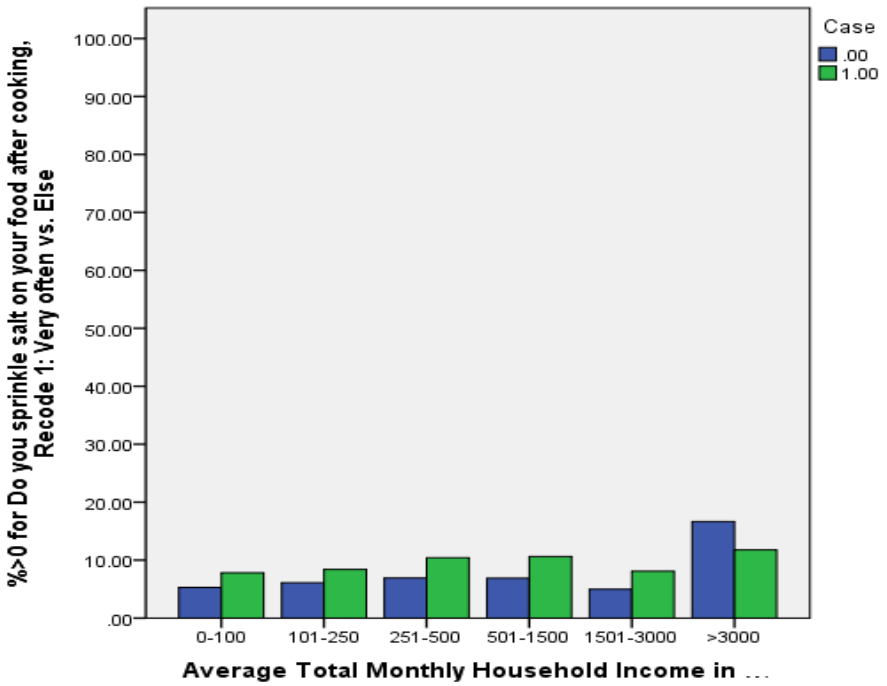


Figure S5A. A graph showing a comparison of average monthly household income and frequency of sprinkling of salt at table among stroke cases and controls.

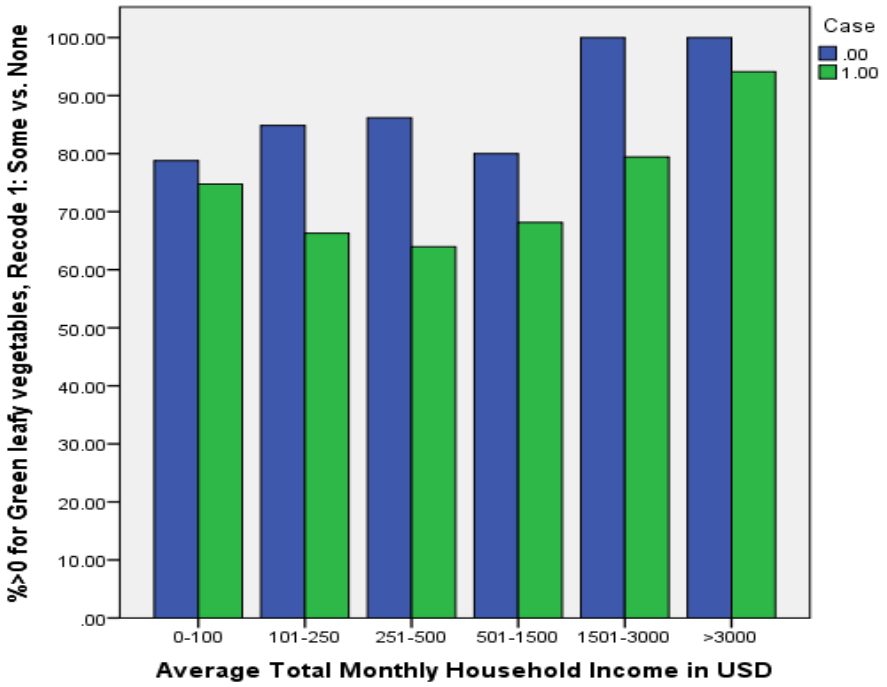


Figure S5B. A graph showing a comparison of average monthly household income and frequency of regular consumption of green leafy vegetables among stroke cases and controls. There is a U-shaped relationship among cases between green vegetables and monthly income.

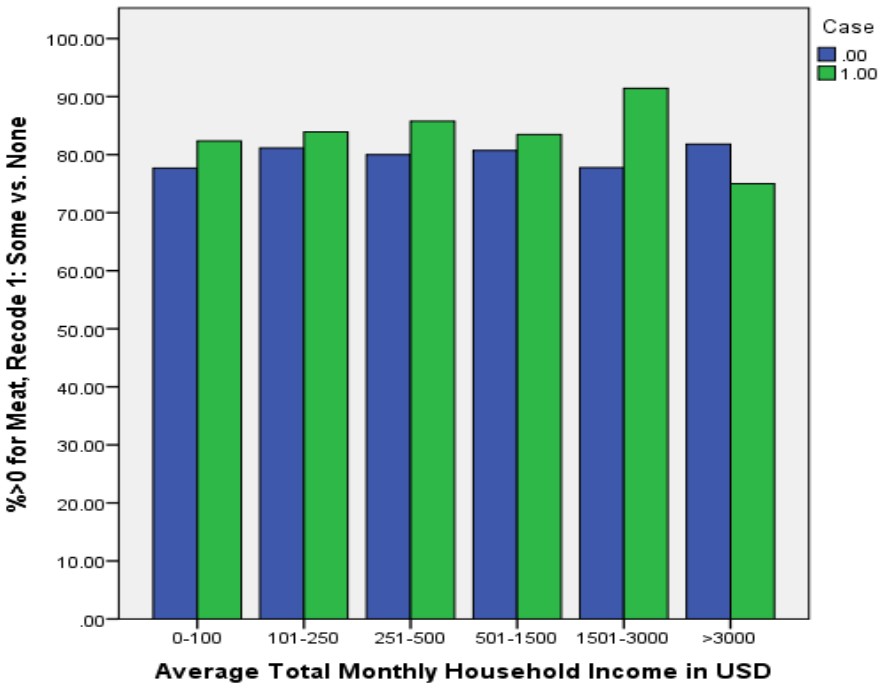


Figure S5C. A graph showing a comparison of average monthly household income and frequency of regular consumption of meat among stroke cases and controls.

Table S14. Risk factors for Hemorrhagic stroke with ischemic stroke as reference.

Risk factor	Adjusted Odds ratio	95% CI for OR Lower	Upper	P-value
Age	0.95	0.94	0.96	<0.001
Education	1.24	0.86	1.79	0.257
Average monthly income	0.87	0.68	1.12	0.277
Hypertension	6.49	3.01	14.02	<0.001
Dyslipidaemia	0.74	0.56	0.97	0.029
Diabetes	0.55	0.42	0.70	<0.001
Cardiac diseases	0.46	0.30	0.70	<0.001
Waist-to-hip ratio	0.37	0.07	1.82	0.22
Physical Activity (some activity)	0.89	0.49	1.59	0.688
Tobacco use in past 12 months	1.34	0.74	2.45	0.335
Alcohol (current user)	1.50	1.14	1.99	0.004
Stress	0.87	0.65	1.16	0.335
Depression	1.16	0.76	1.77	0.492
Family history of cardiovascular diseases	1.11	0.87	1.41	0.409
Adding salt at table	1.11	0.75	1.65	0.588
Green vegetable consumption	1.02	0.79	1.33	0.882
Sugar consumption	0.90	0.70	1.15	0.401
Meat consumption	1.00	0.72	1.38	0.999

APPENDIX: RISK FACTOR DEFINITIONS AND MEASUREMENTS

Hypertension: We measured blood pressure using a standard sphygmomanometer (Omron or Accoson England mercury sphygmomanometer). Systolic blood pressure was determined by Korotkoff phase 1 while diastolic pressure was recorded at Korotkoff phase V. Subject was resting for ≥5 minutes, and had not smoked for at least 30 minutes before the measurement. We ensured an adequate cuff size with bladder encircling and covering 2/3 of length of arm with the bladder over the brachial artery and the lower border should be 1 inch (2-3cm) above the antecubital space. The bladder was deflated slowly and exact values to the nearest 2mmHg were recorded.

Blood pressure (average of three measurements used) was recorded at time of admission (from patient's medical notes), the morning after admission (from patient's medical notes) and daily for 7 days or until death. At time of interview blood pressure was again measured by research personnel using an automated blood pressure monitor. A cutoff of ≥140/ 90 mmHg for up to 72 hours after stroke, a history of hypertension, or use of antihypertensive drugs before stroke or >72 hours after stroke were regarded as indicators of hypertension. Adjustments to systolic BP based on reported associations between pre-morbid BP and acute post-stroke pressure in the Oxford Vascular Study (OXVASC)[8] were applied. Definition of hypertension in controls was self-reported history of hypertension or BP at time of interview ≥140/90mmHg.

In our primary analysis, we used the average of three blood pressure readings taken at admission, day 1 after admission and at interview. Typically stroke subjects present for care late after about 72 hours of stroke onset during which time the acute rise in blood pressure in response to stroke may have started to subside. In sensitivity analysis, we applied an adjustment factor of 0.8755 to systolic blood pressure for hemorrhagic stroke at presentation, day 1 and time of interview and a factor of 0.9358 to systolic blood pressure for ischemic stroke at presentation, day 1 and

time of interview.[8] Hence we calculated the adjusted odds ratio using the mean of three blood pressure measurements (at time of admission, morning after admission and time of interview) as primary analysis and compared with an approach using adjusted blood pressure at time of interview or introduction of new antihypertensive therapy after stroke (see Supplementary table 9)

Weight: The scales were standardized to 0 before each use. Weight was measured in undergarments using a platform scale to the nearest 0.2kg. We recorded the participant's weight twice in kilogram (kg).

Height: We recorded the participant's height in meters (cm). If the participant was able to stand, standing height was measured with the subject bare footed, back square against the bed and eyes looking straight ahead. Supine height was measured with the subject in bare feet, lying on their back square against the bed and eyes looking straight upward. Height was measured to the nearest 0.5cm.

Body Mass Index (BMI): This was calculated by dividing weight (in kg) by square of the height (in meters).

Waist and hip circumferences were measured in the standing and supine positions in cases and controls. Where cases were unable to stand due to disability, these measurements were conducted in the supine position only. Standing waist and hip measurements were used in the present analysis where available. However for cases with only supine estimates, we used the supine measures in the matched control.

Waist circumference: This was measured to the nearest 0.1cm using a non-stretchable standard tape measure attached to a spring balance exerting a force of 750gm over the unclothed abdomen at the midway between the costal margin and the iliac crest. The tape measure was kept horizontal for standing measurement and vertical for supine measurement with the subject relaxed with arms held loosely at sides.

Hip circumference: This was measured to the nearest 0.1cm using a non-stretchable standard tape measure attached to a spring balance exerting a force of 750gm. Measurements were taken over light clothing at the level of the greater trochanters (usually the widest diameter around the buttocks). The tape measure was kept horizontal for standing measurement and vertical for supine measurements.

For waist-to-hip ratio (WHR) and body mass index (BMI), tertiles by sex were calculated based on the overall control data or by using WHO cut-offs[9].

For **psychosocial factors**, we used a combined measure of psychosocial stress employed in INTERHEART[10] and INTERSTROKE[4], which combined self report of stress at home or and work, life events and depression. Psychosocial stress at home/work was defined as the experience, in the two weeks prior to the stroke, of irritability, anxiety, or sleep difficulties as a result of conditions at work or home. For life events, respondents were asked to give a 'yes' or 'no' response to questions about whether, in the two weeks before the stroke, they experienced a stressful life event such as the death of a spouse, death/major illness of a close family member, marital separation/divorce, major personal injury or illness, loss of crop, loss of job/retirement, business failure, major intra-family conflict, violence (including kidnapping, assault, theft, etc.), financial stress, home-related stress, work-related stress, or other major stress.

For the assessment of depression, respondents were first screened for the presence of depressed mood in the four weeks before the stroke. Those who answered in the affirmative were next asked if, for at least two weeks during the four- week period before the stroke, they also experienced at least four out of seven other depression symptoms: loss of interest, feeling tired or low on energy, significant changes in weight, trouble falling asleep as usual, difficulty concentrating, thoughts of death, or feelings of worthlessness.

Dietary History: We evaluated whether or not subjects consumed cooking oil, vegetable intake, sprinkling salt at table, meat consumption, fruits, whole grains, refined grains, dairy products, poultry, eggs, fish and seafood, legumes, prickled food, deep fried foods, salty snacks, confectionary and carbonated beverages. For each of the food items, subjects had to record the number of times it was consumed per month or per week or per day. Regular consumption of a food item was defined as intake of at least once a day, a week, or a month whilst consumption rates less than once a month or never was defined as 'not regular'.

Determination of blood glucose level, HBA1c and lipid profile:

Blood samples were collected from each case within 10 days of symptom onset, and from each control upon enrollment after an overnight fast and into relevant anticoagulant bottles tubes. All blood samples collected were centrifuged at 3000rpm for 20 minutes (2,500rpm for samples in Sodium citrate tubes) and separated into relevant fractions [serum, plasma, buffy coat and red cell concentrates] within 2 hours of collection. Fractions were stored at -20^{o}C in non-self defrosting freezers at peripheral sites before transfer to central biorepository. A daily temperature chart was kept on every freezer to monitor the freezer temperature in order to maintain the samples' integrity

Spot determination of plasma glucose level was carried out across all study sites using the ACCU-CHEK Active Blood Glucose Monitoring Device (Roche Diagnostics, GmBH, Germany), the principle of which was based on the reaction of blood glucose with glucose dehydrogenase enzyme resulting in colour changes which the meter converted to numerical values. Values obtained in mg/dl were converted to mmol/L[11].

Glycated haemoglobin (HbA1c) level was also determined on whole blood from all subjects within 24 hours of sample collection using the Clover A1c Test Catridge System (Infopia Co. Ltd., Korea). The Clover A1c system uses the principle of boronate affinity chromatographic method for the determination of HbA1c in whole blood.[12] Reagents in the system lyse red cells and bind haemoglobin, also the boronate resins bind the cis-doils of glycated haemoglobin. These are measured separately within the system and the ratio of glycated haemoglobin to total haemoglobin were expressed as percentage.

Fasting lipid profile of subjects was determined by quantitative determination of cholesterol, triglycerides, HDL cholesterol using commercially available kits (Randox Laboratories Ltd., UK; Biolabo S.A., France) and the LDL cholesterol was calculated using Friedwald equation.[13] Cholesterol and Triglycerides were determined using the enzymatic hydrolysis/colorimetric method while HDL-cholesterol was determined by precipitation method and the cholesterol fraction measured as previously described.[14-16] Values obtained in mg/dl were converted to mmol/L.[17]

To ensure equivalence across all sites, a standard operating procedure (SOP) was developed on the above laboratory tests and applied across all SIREN sites after a 3- day hands-on-training involving laboratory scientists from across all sites. Refresher trainings were also organized every year. The same brand of test equipment, reagents and test strips were procured and utilized across study sites.

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