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A comparative analysis of risk factors for stroke in blacks and whites: The Atherosclerosis Risk in Communities (ARIC) Study

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Abstract

Objective—Previous studies have speculated that the higher stroke incidence rate in blacks compared with whites may be due, in part, to stroke risk factors exerting a more adverse effect among blacks than whites. To determine whether such racial differences exist we compared the prospective associations between novel, traditional and emerging stroke risk factors in blacks and whites.

Design—Baseline characteristics on risk factor levels were obtained on 15,407 participants from the Atherosclerosis Risk in Communities Study. Stroke incidence was ascertained from 1987–2008. Adjusted Cox proportional hazard models were used to compute hazard ratios (HRs) and their 95% confidence intervals (CIs) for stroke in relation to stroke risk factor levels stratified by race.

Results—During follow-up 988 stroke events occurred: Blacks had higher stroke incident rates compared with whites with the greatest difference in those aged <60 years: 4.34, 3.24, 1.20 and 0.84 per 1,000 person-years, in black men, black women, white men and white women, respectively. Associations between risk factors with incident stroke were similar in blacks and whites excluding diabetes which was more strongly associated with risk of stroke in blacks than in whites: HR 2.54 (95% CI: 2.03–3.18) vs. 1.74 (1.37–2.21), respectively; p for race interaction=0.02.

Conclusions—At all ages, blacks are at considerably higher risk of incident stroke compared with whites, although the effect is most marked in younger age groups. This is most likely due to blacks having a greater burden of stroke risk factors rather than there being any substantial race differences in the associations between risk factors and stroke outcomes.

CONFLICT OF INTEREST
There are no conflicts of interest to declare

Keywords

Stroke; risk factors; racial differences

INTRODUCTION

Over a decade ago, a review of risk factors for stroke in blacks concluded that, aside from age, “elevated blood pressure, diabetes mellitus and smoking are the only risk factors for stroke whose status has been firmly established by published data” [1]. Besides a few small cohorts [2,3] most of the evidence behind this statement was derived from the United States (US) National Health and Nutrition Examination Survey Epidemiologic Follow-up Study (NHANES) [4] and the Multiple Risk Factor Intervention Trial (MRFIT) [5]. Since then, several studies, including the Northern Manhattan Stroke Study [6,7], the Women’s Health Initiative [8], the Reasons for Geographical and Racial Differences in Stroke (REGARDS) study [9,10], the Cardiovascular Health Study [11] and the Atherosclerosis Risk in Communities (ARIC) [12] study, have all contributed information about risk factors for stroke in both blacks and whites. Consequently, dyslipidemia, obesity, inflammatory and hemostatic markers and several cardiac abnormalities have since been identified as additional risk factors for stroke in blacks as well as in whites [6–12].

Data from several US epidemiologic studies with clinically confirmed stroke events have shown that the stroke incidence rate is consistently higher in blacks than in whites [13–17]. The widely acknowledged excess stroke risk among blacks has largely been ascribed to the much higher prevalence of the aforementioned risk factors – particularly diabetes and elevated blood pressure – in the black population compared with whites [18–19]. It has been speculated however, that some of the residual excess stroke risk may be due to a greater impact of risk factors on stroke risk in blacks than in whites [20,21] or even racial differences in more novel stroke risk factors [22].

The ARIC study is well placed for investigating prospectively whether such differences exist due to its biracial population, and having data on a large number of risk factors, and an adequate number of stroke events to permit reliable inter-racial comparison of stroke risk factors. Here, we focus specifically on those risk factors –socio-demographic, traditional and novel or emerging, many of which have previously been demonstrated to be independently associated with incident stroke in ARIC [12].

METHODS

Study design and participants

The ARIC cohort was selected as a probability sample of 15,792 men and women aged 45–64 years at entry from four US study centers, three of which enumerated and enrolled populations reflective of their respective ethnic compositions. Participants from Washington County, Maryland [MD] and selected suburbs of Minneapolis, Minnesota [MN] were almost exclusively white, while participants from Forsyth County, North Carolina were approximately 85% white and 15% black. The fourth quarter of the ARIC cohort was

sampled exclusively from black residents of Jackson, Mississippi. The recruitment of study participants is described in detail elsewhere [23]. The baseline home interview and clinic examination, conducted from 1987–89, measured various risk factors and cardiovascular conditions. Three study visits occurred subsequently, with a fifth visit in 2011–13. Additionally, participants or their proxy were contacted annually by telephone to ascertain hospitalizations and death. Active surveillance of the ARIC community hospitals was also conducted. The ARIC Study protocol was approved by the institutional review board of each participating university and informed consent was obtained from each study participant.

Measurement of baseline risk factors

The risk factors selected have all been previously demonstrated to have a significant association with risk of stroke in the full ARIC population [12]. They were further categorized into socio-demographic, traditional or novel or emerging. Socio-demographic variables included: age, study site, income and educational attainment. Traditional risk factors included: systolic blood pressure (SBP), body mass index (BMI), low-density lipoprotein cholesterol (LDL-c), cigarette smoking, diabetes, and coronary heart disease (CHD). Novel or emerging risk factors included: waist:hip ratio (WHR), high-density lipoprotein cholesterol (HDL-c), albumin, von Willebrand factor, protein C, lipoprotein (a) protein [Lp(a)], white blood cell count (WBC), factor VIIIc, fibrinogen, carotid artery wall thickness, peripheral arterial disease (PAD), left ventricular hypertrophy (LVH) by electrocardiogram (ECG), and physical inactivity. As there was an insufficient number of blacks with prevalent AF (n = 4) to facilitate a racial comparison at Visit 1 we used Visit 4 (1996–1998) as baseline for the analysis of the association between atrial fibrillation and risk of incident stroke. Consequently, the analysis of atrial fibrillation and risk of incident stroke was based on data from a reduced number of 10,400 (2090 blacks) ARIC participants and stroke events (429; 31% blacks).

Baseline assessment

Race/ethnicity was accessed by self-report. Detailed methods have been reported elsewhere for blood collection and for centralized measurement of plasma HDL-cholesterol, LDL-cholesterol, Lp(a) protein [24], fibrinogen, factor VIIIc, von Willebrand factor [25], WBC, albumin, and protein C [26]. Methods used for ascertainment of BMI (weight(kg)/height $(m)^2$) and WHR, SBP, sport physical activity, education and income have been reported elsewhere [27]. A centrally read 12-lead ECG was used to define LVH [28] using the Cornell score. Use of antihypertensive medication within the two weeks before baseline was self-reported [27]. Hypertension was defined as SBP > 140 mmHg or diastolic blood pressure > 90 mmHg or use of antihypertensive medication. PAD was defined as an ankle brachial index less than 0.90 for men and less than 0.85 for women. Smoking status was obtained from the interview [27]. Prevalent diabetes mellitus was defined as a fasting glucose level >126 mg/dl, a nonfasting glucose level >200 mg/dl, a self-reported physician diagnosis, or pharmacologic treatment. Carotid intima-media thickness (IMT) was measured via ultrasound using a standardized protocol [29]. Prevalent CHD included individuals with a history of myocardial infarction (MI), MI adjudicated from the baseline ECG, or history of coronary bypass or angioplasty [30]. Atrial fibrillation was diagnosed from three sources: ECGs done at Visit 4, presence of an International Classification of Disease (ICD9) code for

AF (427.31 or 427.32) in a hospital discharge, or AF listed as any cause of death on a death certificate.

Outcomes

Stroke events and deaths after baseline were identified by local hospital surveillance and annual telephone contact with ARIC participants [31,32]. Hospital records were abstracted and death certificates obtained, and events were classified by a combination of computer algorithm and physician review. Strokes were classified according to published criteria based on the occurrence and duration of neurological signs and symptoms, the results of neuroimaging and other diagnostic procedures, and treatments provided [31]. Strokes secondary to trauma, neoplasm, hematological abnormality, infection, or vasculitis were not counted, and a focal deficit lasting < 24 hours was not considered a stroke. A stroke was classified as ischemic when neuroimaging showed acute infarction or no evidence of hemorrhage.

Statistical Analyses

Of 15,792 ARIC participants at baseline 385 individuals were excluded for the following reasons: participants not of white or black race (n = 48); blacks from MN or MD (n = 55) because of an inability to make inferences to these groups due to small numbers; and 282 (44% black) individuals with missing or prior stroke status. Consequently, 15,407 (27% black) participants remained and contributed to the analysis. The primary outcome was incident stroke (ischemic and hemorrhagic) and the follow-up time was calculated as the time elapsed from the baseline examination (1987–1989) to the date of incident stroke, death, loss to follow-up, or, otherwise, through the end of 2008. Incidence rates per 1000 population person-years by age group (< 60, 60 – 69, and ≥ 70 years), sex and race were calculated by dividing the number of strokes by the number of person-years. Age-group stratification was according to ages when events and person-years accrued (not baseline age). Using Cox proportional hazards regression, the adjusted hazard ratios (HRs) and their 95% confidence intervals (CIs) for both total and ischemic stroke in relation to stroke risk factor levels were computed. Multiplicative interactions for each exposure with race were tested by running models that included the exposure, a race term, and the interaction term, which was a cross-product term with race and the exposure variable of interest. Regardless of whether significant interactions were observed, given inherent interest, we also report the results of race-stratified models. The unit change for each of the continuous risk factors approximated a one standard deviation to facilitate comparison in the magnitude of the association with stroke risk across risk factors.

Two models were computed. Model 1 was adjusted by age and sex. Model 2 adjusted for age, sex, education (< high school, high school graduate and/or vocational school, college, graduate or professional school) and income (< $16,000; $16,000 – $34,999; $35,000 – $49,999; ≥ $50,000; Unknown/Refused). Model 2 also included adjustment for those covariates that may act as confounders (but not mediators) of the association between the exposure of interest and stroke, and which included where appropriate: BMI (continuous), smoking status (current, former, never), SBP (continuous), antihypertensive medication use (yes, no), diabetes (yes, no), HDL-cholesterol (continuous), LDL-cholesterol (continuous),

lipid medication use (yes, no), CHD, PAD, ECG-LVH, carotid IMT and physical activity (ideal, intermediate, poor). Physical activity was categorized by the American Heart Association's ideal CVD health guidelines [33]: Ideal physical activity was defined as ≥150 min/wk moderate or ≥ 75 min/wk vigorous or ≥ 150 min/wk moderate + vigorous activity; intermediate as 1–149 min/wk moderate or 1–74 min/wk vigorous or 1–149 min/wk moderate + vigorous activity; and poor physical activity as 0 min/wk of activity.

Individuals with missing information on the exposure of interest were excluded from the analysis pertaining to that variable, otherwise they were included. The proportional hazards assumption was not violated, confirmed by qualitatively verifying that ln(−ln) survival curves for incident stroke were parallel by stroke risk factor levels (continuous variables were split into tertiles). To test for non-linearity a quadratic model was fitted by adding a squared exposure term to Model 2. Where the squared exposure term was significant at $p < 0.05$, the exposure was represented as quartiles rather than continuous.

RESULTS

The baseline characteristics of study participants according to race and sex are shown in Table 1. There were noticeable differences in the mean and prevalence of certain traditional and more novel or emerging risk factors between blacks and whites; for example, compared with their white counterparts, black men and women had higher mean levels of SBP, Factor VIIIc and Lp(a) protein, and a higher prevalence of diabetes, LVH, and physical inactivity whereas the prevalence of atrial fibrillation at Visit 4 was higher in whites than in blacks.

Over a mean follow-up time of 17.8 years (274 299 person-years), 988 participants had stroke events (415 blacks and 573 whites). Ischemic strokes comprised 88% and the remainder (n = 117) was hemorrhagic in origin that disproportionately occurred in blacks (n = 52). The IR for stroke varied substantially across the race, age and sex-groups with the highest rates observed in black men and the lowest rates in white women at all ages (Figure 1). The difference in stroke rates between blacks and whites was most apparent in those aged < 60 years where black men and women had about four-times the stroke risk compared with whites: IR 4.34, 3.45, 1.20, 0.84 per 1000 person-years in black men, black women, white men and white women, respectively. Thereafter, the difference in stroke rate between blacks and whites diminished but remained higher in blacks compared with whites. Moreover, although low-income level (<$35,000) was associated with increased stroke IR in blacks and whites at all ages, the effect of low income was consistently stronger in blacks at all ages compared with whites (Table 2): blacks with a total household income < $35,000 had stroke IR that were 258%, 141% and 40% higher at ages < 60 yrs, 60–69 yrs and > 70 yrs compared with low income whites. These differences were more extreme than were observed in those with household incomes > $35,000 (196%, 84% and −16%, respectively).

Table 3 shows the adjusted hazard ratios (95% CIs) for the association between an approximate one standard deviation increase (decrease for HDL-cholesterol, serum albumin, and Protein C) in each of the continuous risk factors and the adjusted HRs for the categorical variables with risk of stroke. Of the socio-demographic risk factors, only age and male sex were independently associated with increasing stroke risk in both blacks and whites. Only

for age was there strong evidence of a racial difference: every 5 yr increase in age was associated with a 66% greater risk of stroke in whites compared with a 30% increased risk in blacks (p for interaction = 0.0003). Of the traditional risk factors, SBP, BMI, cigarette smoking, diabetes, prevalent CHD and atrial fibrillation were all positively and independently associated with risk of incident stroke in blacks and whites. The magnitude of the associations was broadly consistent in blacks and whites with the possible exception of diabetes, which was more strongly related with incident stroke in blacks than in whites. Compared with those without diabetes, the association between diabetes and stroke in blacks was twice that of whites: HR (95% CI) 2.54 (2.03 – 3.18) vs. 1.74 (1.37 – 2.21); p for race interaction = 0.02. This remained unchanged after restricting the analysis to ischemic stroke: HR 2.84 (95% CI: 2.24 – 3.60) vs. 1.89 (1.48 – 2.41) p for race interaction = 0.02 (Supplementary Table 1).

For LDL-cholesterol and stroke risk there was weak evidence of an interaction with race: for a 40mg/dl increase in LDL-cholesterol, the HR (95% CI) in whites was 1.12 (1.02 1.22) vs. 0.98 (0.89–1.07) in blacks, p for race interaction = 0.06. However, after restricting the analysis to ischemic stroke there was no longer significant evidence of an interaction with race: HR 1.13 (95% CI: 1.03 – 1.24) in whites vs. 1.00 (0.90 – 1.11) in blacks; p for race interaction = 0.10 (Supplementary Table 1).

Most of the novel and emerging risk factors namely, WHR, HDL-c, serum albumin, Protein C, Lp(a) protein, WBC, factor VIIIc, fibrinogen, carotid artery wall thickness, ECG LVH, PAD, and physical inactivity were positively and independently associated with incident stroke in blacks and whites (Table 3). The relationship between von Willebrand factor with incident stroke was non-linear so a comparison of quartiles was performed: in the adjusted model individuals in the top quartile compared with the lowest quartile had an approximate 50% greater risk of stroke in blacks and whites: 1.47 (95% CI: 1.08 – 2.01) and 1.59 (1.24 – 2.05), respectively (Table 3). For all of these risk factors there was no evidence to indicate that the magnitude of the associations differed between blacks and whites. Restricting the analysis to ischemic strokes did not alter these findings (Supplementary Table 1.)

DISCUSSION

The current findings from this large, biracial US cohort confirm the markedly higher incidence rate of stroke in black men and women compared with their white counterparts. The racial difference was most apparent in the youngest age group where the rate of stroke in blacks was four-times higher than in whites. With age, the racial difference diminished but remained higher in blacks compared with whites consistent with other studies of biracial populations[10, 13–17]. For example, in the REGARDS study the risk of incident stroke at age 45 was 2.9 times higher in blacks than in whites whereas at age 65 the risk difference was reduced to 1.6 times greater in blacks compared with whites [10]. Furthermore, low-income level appeared to be more disadvantageous in blacks at all ages compared with whites. It is conceivable that low income may confer a greater risk of stroke among blacks than whites via lifestyle or environmental mechanisms. For example. poor access to healthy food and sub-optimal food choices may be more prevalent in low-income blacks, which may explain in part why blacks are less likely to adhere to the Dietary Approaches to Stop Hypertension

(DASH) diet compared with whites [34]. An early publication from ARIC [17] as well as other cohorts [10, 18, 19], have shown that this racial disparity is most likely driven, in large part, by the higher burden of stroke risk factors, in particular elevated blood pressure and diabetes, among the black population compared with whites. In particular, the much higher prevalence of stroke risk factors in the black population at younger ages compared with whites is the likely explanation for why the impact of ageing in the current study was observed to be significantly weaker in blacks than in whites.

In addition to these two risk factors, the current study confirms the independent associations between a large number of both traditional and more novel and emerging risk factors with incident stroke in both blacks and whites, namely: cigarette smoking, obesity (both global and central), LDL-cholesterol, HDL-cholesterol, serum albumin, von Willebrand factor, protein C, Lp(a) protein, serum uric acid, WBC, factor VIIIc, fibrinogen, carotid artery wall thickness, LVH, PAD, atrial fibrillation and physical inactivity. Overall, the magnitude of the associations was highly comparable in blacks and whites, with the possible exceptions of diabetes and LDL-cholesterol where there was some limited evidence of racial differences in the strength of the relations. However, for these latter risk factors, it is highly possible that the weak interactions with race that we observed were chance findings due to the large number of comparisons performed.

In the current study, diabetes was observed to be a more potent risk factor for incident stroke in blacks compared with whites, a finding which is in agreement with that from the Greater Cincinnati/Northern Kentucky Stroke Study which showed a race-specific effect, with higher risk of ischemic stroke for blacks with diabetes than for their white counterparts [21]. Aside from the role of chance, our finding may be due to underlying physiological differences, differences in the duration or severity of diabetes, or to racial disparities in the efficacy, adherence or use of anti-diabetes medication. In support of this, a meta-analysis of individuals with diabetes showed that blacks had on average 0.65% higher HbA1c compared with whites, which the authors suggested may contribute to the excess diabetes related mortality in the black population [35]. It should be noted however, that data from NHANES – the only other study to have reported on the interaction between diabetes and stroke risk by race -suggested no such interaction [19]. Given the uncertainty around the issue, as well as the greater burden of diabetes in the black population, future studies that are able to confirm or refute a racial difference between diabetes and stroke risk are warranted.

The presence of a weak association between LDL-cholesterol level and stroke risk – and in particular ischemic stroke - is consistent with several meta-analyses of observational studies [36] and randomized trials of cholesterol lowering medications [37]. In the current study, the relation between LDL-cholesterol and risk of total stroke was confined to whites. After excluding hemorrhagic strokes for which there is a null (or inverse) association with LDL-cholesterol, and which disproportionately occurred in blacks, there was no longer any support for a racial difference. This finding receives some support from the Justification for the Use of Statins in Prevention trial [38]. In that study, there was a non-significant reduction in the relative risk of stroke in blacks with cholesterol lowering (HR 0.56 95% CI: 0.19 – 1.60) that was consistent with the significant 45% reduction seen overall. However, given that the randomized analysis was based on fifteen stroke events among blacks, more

evidence is required before any definitive conclusions regarding the relationship between LDL-cholesterol and stroke risk in blacks can be reached.

The principal limitation of this analysis relates to the lack of overlap between black and whites at the four study sites. As most of the black participants were recruited from the Jackson, Mississippi field center and the whites from the other three sites, we cannot preclude confounding of race comparisons by unmeasured factors related to geography or study center. Second, the biomarkers were assayed using a single measurement that may have resulted in misclassification of the usual levels of these risk factors in some individuals and hence, a dilution in the strength of the association with stroke risk. However, as misclassification is likely to have been randomly distributed across blacks and whites, it is unlikely to have impacted materially on the racial comparison. Finally, as there were only 19 cases of atrial fibrillation among blacks at Visit 4 (compared with 255 in whites) the comparative analysis of the association between prevalent atrial fibrillation and stroke risk in blacks and whites is likely to have been underpowered. Thus, although there was no significant evidence of a racial difference between prevalent atrial fibrillation and stroke risk we cannot exclude the possibility that there may indeed be a difference in how atrial fibrillation affects the risk of stroke in blacks and whites.

In summary, the associations between traditional, novel and emerging risk factors with incident stroke are highly consistent in blacks and whites. Therefore, it is unlikely that significant racial differences in the way stroke risk factors operate explain the substantially higher stroke incidence rate in the US black population. An alternate explanation is that the racial disparity is a consequence in part of an interaction between social and biological or behavioral risk factors [39]. Future studies that are able to explore the complex interplay between social factors, race, and stroke risk are warranted.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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KEY MESSAGES

- The incidence rate of stroke in black men and women is substantially higher than in whites with the racial difference being most pronounced in the youngest age-groups where the rate of stroke in blacks was four-times higher than in whites.
- Low-income level appears to be associated with greater incidence of stroke at all ages in blacks than whites.
- Given that the associations between traditional, novel and emerging risk factors with incident stroke are highly consistent in blacks and whites the substantially higher stroke incidence rate observed in blacks compared with whites is most likely a consequence, in part, of socio-economic and behavioral factors rather than any important biological differences between races.

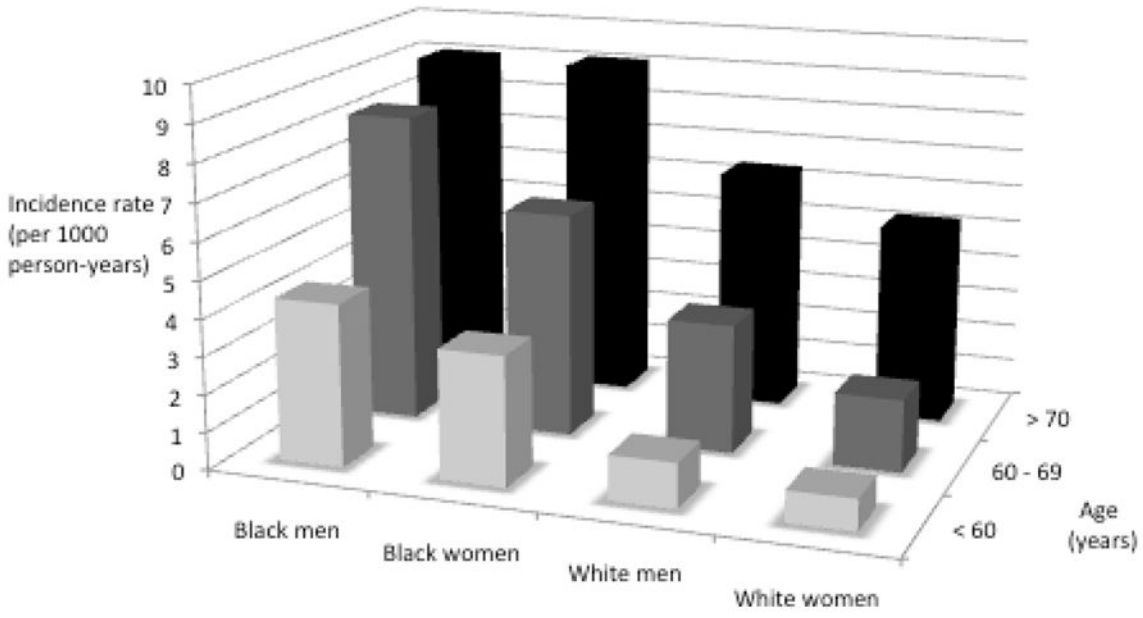

Figure 1.

Incidence rates (IR) per 1,000 population person-years for incident stroke by age at risk, race and sex, in the Atherosclerosis Risk in Communities Study (ARIC) 1987 – 2008.

Table 1

Baseline characteristics (mean and standard deviation, or percent) of study participants free of stroke, by race and sex, and stroke risk factors in ARIC, 1987 – 1989

Variable	Blacks		Whites	
	Men (n=1534)	Women (n = 2552)	Men (n = 5335) (n = 5986)	Women
Socio-demographic				
Age, years	54 (6)	53 (6)	55 (6)	54 (6)
Study site, n (%)				
Forsyth County	189 (12)	277 (11)	1624 (30)	1862 (31)
Jackson	1345 (88)	2275 (89)	0	0
Minneapolis suburbs	0	0	1889 (35)	2039 (34)
Washington County	0	0	1822 (34)	2085 (35)
< High school education, n (%)	669 (44)	1026 (40)	951 (18)	972 (16)
< $35,000 per year income, n (%)	1057 (77)	2011 (87)	2082 (41)	2917 (51)
Traditional				
SBP, mmHg	130 (22)	128 (21)	120 (16)	117(18)
BP-lowering medication, n (%)	530 (35)	1218 (48)	1283 (24)	1585 (27)
BMI (kg/m^2)	28 (5)	31 (7)	27 (4)	27 (6)
LDL-c (mg/dL)	137 (42)	138 (44)	140 (36)	135 (40)
Lipid-lowering medication, n (%)	18 (1)	37 (2)	186 (4)	188 (3)
Current smoker, n (%)	580 (38)	620 (24)	1304 (25)	1486 (25)
Diabetes, n (%)	268 (18)	504 (20)	532 (10)	477 (8)
Diabetes medication, n (%)	157 (10)	287 (11)	195 (4)	188 (3)
CHD, n (%)	77 (5)	66 (3)	449 (9)	103 (2)
Atrial fibrillation(%)[a]	9 (1)	10 (0.6)	169 (4)	86 (1.8)
Novel or emerging				
Waist:hip ratio	0.9 (0.1)	0.9(0.1)	1.0 (0.1)	0.9 (0.1)
HDL-c (mg/dL)	51 (17)	58 (17)	43 (12)	58 (17)
Serum albumin (g/dL)	3.9 (0.3)	3.8 (0.3)	3.9 (0.2)	3.9 (0.3)
von Willebrand factor (%)	131 (55)	136 (59)	114 (44)	111 (42)
Protein C, μg/mL	3.0 (0.6)	3.2 (0.6)	3.1 (0.6)	3.3 (0.7)

Variable	Blacks		Whites	
	Men (n=1534)	Women (n = 2552)	Men (n = 5335) (n = 5986)	Women
Lp(a)protein, μg/mL	147 (112)	168 (128)	75 (88)	86 (97)
WBC (10^3 cells/mm^3)	5.6 (2.0)	5.7 (2.0)	6.4 (2.1)	6.1 (1.9)
Factor VIIIc (%)	142 (45)	151 (50)	123 (34)	128 (35)
Fibrinogen (mg/dL)	307 (70)	328 (72)	295 (63)	300 (61)
Carotid IMT (mm)	0.76(0.18)	0.71(0.15)	0.78 (0.20)	0.67 (0.16)
ECG LVH, n (%)	85 (6)	131 (5)	56 (1)	55 (1)
PAD, n (%)	61 (4)	73 (3)	126 (3)	121 (2)
Poor physical activity, n (%)	835 (55)	1541 (60)	1574 (30)	1905 (32)

Abbreviations: ARIC = Atherosclerosis Risk in Communities Study; SBP = systolic blood pressure; BMI = body mass index; LDL-c = low-density lipoprotein cholesterol; WHR = waist:hip ratio; HDL-c = high-density lipoprotein cholesterol; Lp(a) protein = lipoprotein (a); WBC = white blood cells; CHD = coronary heart disease; IMT= intima media thickness; ECG-LVH = electrocardiogram left ventricular hypertrophy; PAD = peripheral arterial disease; a = Baseline for the analysis of atrial fibrillation was Visit 4 (1996–1998)

Table 2

Incidence rates per 1,000 population person-years for incident stroke by age, income level and race, ARIC, 1987–2008

Population	Age-group								
	< 60 years			60 – 69 years			≥ 70 years		
	IR (95% CI)	N	Person- years	IR (95% CI)	N	Person- years	IR (95% CI)	N	Person- years
Blacks <$35,000 per year	4.26 (3.40, 5.27)	80	18791	7.42 (6.35, 8.61)	166	22381	9.24 (7.46, 11.3)	88	9522
Blacks ≥$35,000 per year	2.76 (1.61, 4.44)	15	5433	3.97 (2.44, 6.14)	18	4531	4.18 (1.59, 9.16)	5	1196
Whites <$35,000 per year	1.19 (0.82, 1.69)	29	24269	3.08 (2.57, 3.66)	122	39623	6.62 (5.65, 7.71)	158	23870
Whites ≥$35,000 per year	0.93 (0.67, 1.26)	38	40876	2.16 (1.78, 2.61)	104	48108	5.00 (4.09, 6.06)	99	19785

Abbreviations: ARIC = Atherosclerosis Risk in Communities Study; IR = Incidence rate; 95% CI = 95% Confidence Interval

Table 3

Adjusted hazard ratios (95% confidence intervals) for incident total stroke and risk factors for stroke by race*, ARIC, 1987–2008

Risk factor	Unit change (~1 SD)	Age and sex-adjusted			Confounder-adjusted		
		Blacks (n=415)	Whites (n=573)	P-value for interaction	Blacks (n=375)	Whites (n=551)	P-value for interaction
Socio-demographic							
Age [a]	5	1.36 (1.25, 1.47)	1.67 (1.55, 1.80)	0.0004	1.30 (1.19, 1.42)	1.66 (1.53, 1.80)	0.0003
Sex [b]	Men vs women	1.23 (1.01, 1.50)	1.43 (1.21, 1.68)	0.24	1.39 (1.12, 1.74)	1.50 (1.25, 1.78)	0.31
Income [c]							
< $16,000	Vs. > $50,000	2.76 (1.53, 4.97)	1.94 (1.46, 2.57)		1.45 (0.67, 3.18)	1.43 (1.01, 2.01)	
$16,000 – $34,999		1.89 (1.03, 3.44)	1.54 (1.22, 1.96)	0.82	1.52 (0.71, 3.26)	1.24 (0.93, 1.64)	0.64
$35,000 – $49,999		1.59 (0.80, 3.14)	1.54 (1.19, 1.98)		1.47 (0.64, 3.38)	1.48 (1.11, 1.97)	
P for trend		< 0.0001	< 0.0001		0.66	0.13	
Education [d]							
< High school	Vs.<graduate or professional school	2.49 (1.69, 3.67)	1.51 (1.07, 2.13)		1.79 (1.06, 3.02)	0.83 (0.56, 1.23)	
HS graduate and/or vocational school		1.75 (1.16, 2.64)	1.25 (0.90, 1.73)	0.42	1.53 (0.90, 2.61)	0.81 (0.57, 1.17)	0.07
College		1.58 (1.01, 2.46)	1.02 (0.72, 1.43)		1.44 (0.83, 2.50)	0.72 (0.50, 1.05)	
P for trend		< 0.0001	0.0008		0.03	0.98	
Traditional							
SBP (mmHg) [e]	20	1.44 (1.34, 1.55)	1.38 (1.26, 1.51)	0.94	1.41 (1.30, 1.53)	1.38 (1.26, 1.52)	0.87
BMI (kg/m^2) [f]	5	1.13 (1.05, 1.23)	1.13 (1.03, 1.23)	0.77	1.13 (1.05, 1.23)	1.16 (1.06, 1.26)	0.56
LDL-c (mg/dL) [g]	40	1.00 (0.91, 1.10)	1.15 (1.05, 1.25)	0.01	0.98 (0.89, 1.07)	1.12 (1.02, 1.22)	0.06
Cigarette smoking [h]	C vs. Never	1.41 (1.13, 1.77)	1.85 (1.52, 2.27)	0.24	1.31 (1.04, 1.64)	1.77 (1.44, 2.17)	0.29
Former smoker [h]	F vs. Never	0.93 (0.72, 1.21)	0.96 (0.78, 1.18)		0.89 (0.69, 1.16)	0.96 (0.78, 1.18)	
BP-lowering medication [i]	Yes vs. No	1.74 (1.42, 2.12)	1.86 (1.57, 2.20)	0.37	1.32 (1.06, 1.63)	1.64 (1.37, 1.97)	0.35
Lipid-lowering medication [j]	Yes vs. No	0.97 (0.43, 2.17)	1.05 (0.68, 1.62)	0.75	1.04 (0.43, 2.53)	0.90 (0.57, 1.43)	1.00
Diabetes [k]	Yes vs. No	3.05 (2.48, 3.74)	2.23 (1.80, 2.77)	0.09	2.54 (2.03, 3.18)	1.74 (1.37, 2.21)	0.02
CHD [l]	Yes vs. No	2.17 (1.45, 3.23)	1.92 (1.44, 2.58)	0.91	1.61 (1.04, 2.50)	1.66 (1.22, 2.26)	0.76
Atrial fibrillation [m]	Yes vs. No	2.07 (0.51, 8.36)	2.63 (1.75, 3.95)	0.73	1.13 (0.29, 2.16)	2.20 (1.43, 3.39)	0.96

Risk factor	Unit change (~1 SD)	Age and sex-adjusted			Confounder-adjusted		
		Blacks (n=415)	Whites (n=573)	P-value for interaction	Blacks (n=375)	Whites (n=551)	P-value for interaction
Novel or emerging							
WHR [f]	0.10	1.45 (1.26,1.67)	1.45 (1.27,1.64)	0.59	1.36 (1.18, 1.57)	1.39 (1.22, 1.58)	0.61
HDL-c (mg/dL) [g]	−20	1.34 (1.17, 1.53)	1.25 (1.11, 1.41)	0.60	1.20 (1.04, 1.37)	1.01 (0.89, 1.14)	0.09
Serum albumin (g/dL) [n]	−0.3	1.40 (1.26, 1.56)	1.20 (1.08,1.32)	0.03	1.30 (1.17, 1.44)	1.22 (1.10, 1.36)	0.22
Protein C (μg/mL) [n]	−0.6	1.10 (1.00,1.22)	0.97 (0.90,1.06)	0.07	1.15 (1.04, 1.28)	1.03 (0.94, 1.13)	0.09
von Willebrand factor (%) [n]	4th vs. 1st quartile	1.66 (1.24, 2.23)	1.74 (1.36, 2.23)	0.3	1.47 (1.08, 2.01)	1.59 (1.24, 2.05)	0.67
Lp(a) protein (μg/mL)[n]	107	1.15 (1.06,1.24)	1.12 (1.02, 1.21)	0.53	1.16 (1.06, 1.26)	1.10 (1.01, 1.21)	0.87
WBC (10^3 cells/mm)^3 [n]	2.0	1.19 (1.12, 1.26)	1.15 (1.11, 1.19)	0.26	1.14 (1.05, 1.24)	1.12 (1.05, 1.19)	0.53
Factor VIIIc (%) [n]	40	1.26 (1.17, 1.36)	1.26 (1.16, 1.37)	0.76	1.14 (1.06, 1.24)	1.21 (1.10, 1.34)	0.77
Fibrinogen (mg/dL) [n]	60	1.22 (1.13, 1.32)	1.23 (1.15, 1.32)	0.72	1.10 (1.01, 1.20)	1.11 (1.03, 1.20)	1.00
Carotid IMT (mm) [n]	0.20	1.48 (1.34, 1.63)	1.40 (1.30,1.50)	0.95	1.30 (1.17, 1.45)	1.25 (1.16, 1.35)	0.99
LVH-ECG [n]	Yes vs. No	2.44 (1.79, 3.33)	2.27 (1.32, 4.00)	0.98	1.52 (1.08, 2.17)	1.69 (.94, 3.03)	0.78
PAD [m]	Yes vs. No	1.79 (1.14, 2.82)	2.20 (1.47, 3.29)	0.39	1.44 (0.90, 2.32)	1.57 (1.03, 2.38)	0.63
Physical activity level [o]							
Intermediate	Intermediate vs. Ideal	1.38 (1.00, 1.91)	1.26 (1.05, 1.53)	0.10	1.33 (0.96, 1.84)	0.98 (0.79, 1.21)	0.12
Poor		1.59 (1.21, 2.09)	1.05 (0.85, 1.29)		1.37 (1.04, 1.80)	1.08 (0.89, 1.32)	
P-for trend		0.06	0.68		0.04	0.45	

[*] Multiplicative race-interactions were evaluated by including cross-product terms in the models (dataset contained both blacks and whites). Race-specific HR's were computed from race-stratified analyses (separate models run for blacks and whites). The confounder-adjusted models included the following adjustments:

[a] = sex, education, income, education, smoking, BMI, physical activity (PA);

[b] = age, education, income, education, smoking, BMI, PA;

[c] = age, sex, education, SBP, BP-medication, LDL-c, HDL-c, lipid-medication, smoking, BMI, diabetes, CHD, serum albumin, protein C, VWF, Lp(a) protein, WBC, factor VIIIc, fibrinogen, carotid IMT, PAD, LVH, PA;

[d] = age, sex, income, SBP, BP-medication, LDL-c, HDL-c, lipid-medication, smoking, BMI, diabetes, CHD, serum albumin, protein C, VWF, Lp(a) protein, WBC, factor VIIIc, fibrinogen, carotid IMT, PAD, LVH, PA;

[e] = age, sex, income, education, BP-medication, BMI, LDL-c, HDL-c, lipid-medication, smoking, diabetes, PA;

[f] = age, sex, income, education, smoking, PA;

[g] = age, sex, income, education, SBP, BP-medication, HDL-c, lipid-mediation, smoking, diabetes, PA;

[h] = age, sex, income, education, PA;

[I] = age, sex, income, education, SBP, BMI, LDL-c, HDL-c, lipid-medication, smoking, diabetes, PA;

[j] = age, sex, income, education, SBP, BP-medication, LDL-c, HDL-c, smoking, diabetes, PA;

[k] = age, sex, income, education, SBP, BP-medication, BMI, LDL-c, HDL-c, lipid medication, smoking, PA;

[l] = age, sex, income, education, SBP, BP-medication, BMI, LDL-c, HDL-c, lipid-medication, smoking, diabetes, PA;

[m] = age, sex, income, education, SBP, BP-medication, BMI, LDL-c, HDL-c, lipid-medication, smoking, diabetes, PA, CHD. Baseline for the analysis of atrial fibrillation was Visit 4 (1996–1998);

[n] = age, sex, education, income, SBP, BP-medication, LDL-c, HDL-c, lipid-medication, smoking, BMI, diabetes, PA;

[o] = age, sex, education, income, smoking. Abbreviations as shown in Table 1. C vs Never = current vs. never smoking; F vs. Never = former vs never smoker; HS = high school.