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Racial Differences in the Association between Non-Exercise Estimated Cardiorespiratory Fitness and Incident Stroke

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Abstract

Objective—To examine the association between estimated cardiorespiratory fitness (eCRF) and incident stroke by black and white race. Non-exercise eCRF is a promising alternative to assess CRF though its role as a predictor of incident stroke remains unclear, especially in a black population.

Methods—24,162 participants from the REGARDS study (54.8% women, 39.5% blacks, mean age 64.6 years) without stroke at enrollment 2003–2007 were followed for incident stroke through March 31, 2016. Baseline eCRF in maximal metabolic equivalents (METs) was determined using non-exercise sex-specific algorithms and further grouped into age- and sex- specific tertiles.

Results—Over a mean (SD) of 8.3 (3.2) years of follow-up, 945 incident strokes occurred (377 in black, 568 in white). The association between eCRF and stroke risk differed significantly by race ($P_{\text{Interaction}} < .001$). In whites, after adjustment for stroke risk factors and physical

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functioning, the hazard for stroke was 0.82 (95%CI: 0.67 – 1.00) times lower in the middle tertile of eCRF compared to the lowest, and was 0.54 (95% CI: 0.43 – 0.69) times lower in the highest tertile of eCRF. The protective effect of higher levels of eCRF on stroke incidence was more pronounced in those 60 years or older in whites. No association between eCRF and stroke risk was observed in blacks.

Conclusions—eCRF using non-exercise algorithms is a useful predictor of stroke in whites. The lack of an overall association between eCRF and stroke risk in blacks suggests that assessment of eCRF in blacks may not be helpful in primary stroke prevention.

Keywords

exercise capacity; stroke; REGARDS; race

Introduction

Stroke is the fifth leading cause of death in the United States (U.S.) and the second-leading cause of death globally, accounting for 133,103 deaths in the U.S in 2014. and nearly 6.5 million deaths worldwide in 2013.¹ Identifying modifiable factors has important public health significance for primary stroke prevention.

Cardiorespiratory fitness (CRF), a modifiable factor associated with cardiovascular disease (CVD), can be defined as the ability of the circulatory, respiratory, and muscular systems to supply oxygen during sustained physical activity (PA). A limited number of studies have demonstrated an inverse relationship between CRF and stroke morbidity and mortality.^{2–7} A large meta-analysis has confirmed the risk reduction role that CRF has on stroke.⁸ However, a recent Finnish cohort study of men reported no association between CRF and incident non-fatal stroke.⁹ Furthermore, no studies have included substantial numbers of blacks, despite it being long-established that blacks have higher stroke incidence and mortality than whites in the US.¹⁰ Reasons underlying racial differences in stroke incidence and mortality include, but are not limited to the presence of traditional risk factors (e.g., age, sex, systolic blood pressure, current smoking status, diabetes mellitus) as well as novel risk factors (e.g., inflammation, psychosocial factors, and others).¹¹ Studies have shown there are significant race/ethnic differences in CRF, with lower CRF in blacks than whites.^{12–17} A better understanding of the racial/ethnic contribution to the association between CRF and stroke could help develop better stroke prevention strategies to reduce the unequal distribution of the public health burden of stroke.

CRF is typically expressed as maximal oxygen uptake (VO_2max) in metabolic equivalents (METs) and can be assessed directly or estimated indirectly.¹⁸ It is not routinely measured in clinical practice,¹⁹ nor included in common risk algorithms,^{20–22} probably due to issues with feasibility and cost in most clinical settings. Therefore, non-exercise algorithms have been developed to estimate CRF (eCRF) using variables commonly assessed in public health and clinical settings, and to provide a rapid and inexpensive way of deriving CRF.^{23–30} These non-exercise eCRF assessments are similar in accuracy to CRF predicted from submaximal exercise tests in relatively healthy adults.^{23, 25, 30, 31}

Recent studies have documented significant associations between non-exercise eCRF and long-term health risks, including CVD and all-cause mortality in both middle-aged and older populations.^{32–36} The risk reduction associated with each 1-MET increase in non-exercise eCRF ranges from 7.4% to 21% and 8% to 16.9% for all-cause and CVD mortality, respectively. However, no study has been conducted on the relationship between eCRF and stroke incidence. Therefore, the objective of the present study was to investigate the association between eCRF and incident stroke in a national biracial cohort study of men and women.

Methods

Study Participants

We analyzed data from the REasons for Geographic And Racial Differences in Stroke (REGARDS) study, a national, population-based, longitudinal study of 30,239 American men and women, blacks and whites. The study methods have been reported elsewhere.³⁷ In brief, adults aged 45 years and older from across the U.S. were recruited by mail and telephone between January 2003 and October 2007 with oversampling of blacks and residents of the “buckle” of the stroke belt (coastal plans of NC, SC, and GA) and the rest of the stroke belt (remainder of NC, SC, and GA plus AL, MS, TN, AR, and LA.) The purpose of the REGARDS study was to determine the causes for the excess stroke mortality in blacks and those living in the Southeastern area of the U.S. Institutional review boards of the collaborating institutions approved the study protocol. Participants gave written informed consent for baseline and follow-ups. Demographic, lifestyle factors, and medical history were obtained by telephone interview followed by an in-home visit to obtain an electrocardiography (ECG) and physical measurements. Participants are followed by telephone every 6 months to identify suspected strokes and other medical events.

All participants included in this study were free of stroke at baseline and had complete data to calculate the non-exercise eCRF. We excluded 5,773 individuals based on one or more of the following criteria: previous stroke (n=1930), missing data for calculating non-exercise eCRF (resting heart rate (RHR, n=339); waist circumference (WC, n=170); body mass index (BMI, n=196); smoking (n=105); and PA (n=413)), missing confounder data (n=1706), or lost to follow-up (n=485). Also excluded were those with BMI<18.5 (the non-exercise equation was developed in a population of BMI 18.5³⁰), BMI >80, RHR < 30 bpm or >150 bpm (outliers) (n=752). The final analytical sample was 24,162 adults (54.8% women, 39.5% blacks).

Assessment of Non-exercise eCRF

Non-exercise eCRF at baseline was estimated in METs ($3.5 \text{ mL O}_2 \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$) with the following sex-specific algorithms³⁰:

$$\begin{aligned} \text{eCRF in men (METs)} = & 21.2870 + (0.1654 * \text{age}) - (0.0023 * \text{age}^2) - (0.2318 * \text{BMI}) - (0.0337 * \text{WC}) \\ & - (0.0390 * \text{RHR}) + (0.6351 * \text{physically active}) - (0.4263 * \text{current smoker}) \end{aligned}$$

$$\begin{aligned} \text{eCRF in women (METs)} = & 14.7873 + (0.1159 * \text{age}) - (0.0017 * \text{age}^2) - (0.1534 * \text{BMI}) - (0.0088 * \text{WC}) \\ & - (0.0364 * \text{RHR}) + (0.5987 * \text{physically active}) - (0.2994 * \text{current smoker}) \end{aligned}$$

BMI was calculated from measured height and weight; WC in cm was measured level with the umbilicus; RHR was determined with the participant recumbent after 5-minute of rest and obtained from the resting ECG.³⁸ PA was assessed by a self-reported question that has been well validated: “How many times per week do you engage in intense physical activity enough to work up a sweat?”^{39, 40} Being physically active was classified by the response of 4 times/week.^{41, 42} Participants also reported their smoking status (never smoked, former smokers, or current smokers). Once the algorithms were implemented, participants were classified into lower, middle, and upper groups according to age- (<60 or ≥60 years), and sex- (men or women) specific thirds of the estimated METs distribution.

Identification of Incident Stroke

Ascertainment of stroke was through follow-up telephone interview every 6 months and has been previously described in detail.¹⁰ In brief, reports of any possible stroke, transient ischemic attack (TIA), brain hemorrhage, stroke symptoms, or unknown reason for hospitalization during follow-up generated a request for retrieval of medical records. Medical records were centrally adjudicated by at least two physicians based on the World Health Organization definition.⁴³ Strokes were further classified as ischemic or hemorrhagic. Death certificates and/or proxy interviews were reviewed for deaths without medical records. Reported stroke events through October 2015 were included. For participants who were deceased, the follow-up date was their death date; and for those without stroke, the follow-up date was the most recent contact date up to March 31, 2016.

Potential Confounders

RHR, BMI, WC, smoking status, and PA were used in calculating the non-exercise eCRF in METs; therefore, these variables were not adjusted for in analysis due to the concern of over-adjustment. Participant's highest education was reported as less than high school, high school graduate, some college or college graduate and above. Region was coded as stroke belt, stroke buckle, and non-stroke belt. Heavy alcohol drinker was defined as ≥7 drinks/wk for women and ≥14 drinks/wk for men.⁴⁴ Coronary heart disease (CHD) was defined as self-reported myocardial infarction (MI), coronary artery bypass grafting, angioplasty, or stenting, or evidence of MI via ECG; diabetes mellitus (DM) was defined as self-reported use of oral hypoglycemic medications or insulin, fasting glucose >7.0 mmol/L (126 mg/dL), or non-fasting glucose >11.1 mmol/L (200 mg/dL); dyslipidemia was defined as self-reported use of lipid-lowering medication, total cholesterol ≥6.22 mmol/L (240 mg/dL), low-density lipoprotein cholesterol (LDL) ≥4.14 mmol/L (160 mg/dL), or high-density lipoprotein cholesterol (HDL) <1.04 mmol/L (40 mg/dL); atrial fibrillation (AF) was defined by the study ECG and also from a self-reported medical history of a physician diagnosis during the computer-assisted telephone interview surveys⁴⁵; and left ventricular hypertrophy (LVH) was defined by the Sokolow-Lyon criteria using ECG data.⁴⁶ The physical functioning score, as indexed by the Physical Component Summary Score of the

12-item Short Form Survey (SF-12) was available among 23,520 participants.⁴⁷ SF-12 has been demonstrated to be reliable and valid in several population-based applications.^{48–53}

Statistical Analysis

Baseline characteristics of the study population were characterized by ethnicity and non-exercise eCRF tertiles (lower, middle, and upper). Differences in covariates were tested using student t test and ANOVA for continuous variables and chi-square for categorical variables. Cox proportional hazards models were used to examine the association between non-exercise eCRF and risk of developing stroke. Hazard Ratios (HRs) and 95% confidence intervals (CIs) were reported as an index of the strength of association. The proportional hazards assumptions were met as assessed by comparing the log-log survival plots. Four models were tested: 1) unadjusted-model; 2) sociodemographic-adjusted model, including age, gender, race (blacks vs whites), education, and region; 3) risk factor-adjusted model, including all the variables in model 2 plus systolic blood pressure, self-reported use of antihypertensive medications, heavy alcohol drinker (yes/no), presence of CHD, DM, dyslipidemia, AF, and LVH (yes/no for each); and 4) the final model, adjusted for variables in model 3 plus physical functioning score as a continuous variable for those participants who completed the SF-12. We assessed linear trends in the association of non-exercise eCRF with the risk of total stroke, and stroke type (ischemic and hemorrhagic stroke). We also examined non-exercise eCRF as a continuous variable so that each HR represents the risk associated with a 1-MET increase in the exposure variable. Evidence of interaction was determined by an a priori α level of 0.10. Interactions between sex and non-exercise eCRF tertiles, and race and non-exercise eCRF tertiles were tested and the interaction term was not significant for sex (Wald Chi-square test: $P=0.23$ for overall stroke and $P=0.37$ for ischemic stroke), but significant for race (Wald Chi-square test: $P<0.0001$ for overall stroke and for ischemic stroke). Therefore, the results are presented as pooled analyses for men and women, but race-stratified. However, to facilitate comparisons with other studies^{2, 3, 5–7, 9}, the sex-specific analyses are presented in the Supplement (eTable 1 and eTable2 in the Supplement). We also plotted the receiver operating characteristic(ROC) curves to determine if there was a significant improvement in the predictive accuracy of stroke outcomes by augmenting traditional cardiovascular risk factors and lifestyle factors with eCRF. The chi-square test determined if there was a significant difference between the models. Because of the documented higher stroke incidence for blacks than whites at younger ages⁵⁴, we performed exploratory analyses on total stroke across older (≥ 60 yrs) and younger (<60 yrs) groups. Analyses were conducted using SAS, version 9.4 with alpha set at $P<0.05$.

Results

Among the 24,162 participants, 945 (3.9%) developed stroke (377 in black, 568 in white; 842 ischemic and 103 hemorrhagic) during an average of 8.3 ± 3.2 years of follow-up. Baseline characteristics are presented by ethnicity in Table 1 and eCRF tertiles in Table 2. Overall, participants had a mean age of 64.6 years and BMI of 29.4 kg/m^2 , and 44% resided in the non-stroke belt. Blacks were younger, less educated, more likely to be women, had higher BMI and waist circumference, and unfavorable blood lipids, glucose, blood pressure, and higher prevalence of chronic diseases than whites. Participants in the lower tertile were

also older, less educated, more likely to be black, more likely to be smokers, were less physically active, and had higher BMI, unfavorable blood lipids and glucose, and higher prevalence of chronic diseases than those in the higher eCRF group.

Due to the significant interaction between race and eCRF, race-stratified results are presented (Table 3). For whites, in the age, gender, education and region-adjusted model, an inverse association was observed between higher levels of eCRF and incident stroke. Those in the middle and upper tertile of eCRF had 36% and 63% lower risk of developing any stroke, respectively, compared to those in the lower tertile. Each 1-MET increment in eCRF was associated with a 21% lower risk of incident stroke. Additional adjustment for other traditional stroke risk factors and physical functioning score did not significantly change the associations; the HRs changed only slightly and the association remained. In the fully adjusted model (model 4), for whites, the HR (95% CI) ranged from 0.82 (0.67-1.00) in the middle tertile to 0.54 (0.43-0.69) in the upper tertile ($P<.001$ for linear trend). For blacks, there was no association between levels of eCRF and incident stroke in any of the models examined. In the fully adjusted model, the HR (95% CI) ranged from 1.07 (0.84-1.37) in the middle tertile to 1.09 (0.82-1.45) in the upper tertile ($P=.54$ for linear trend). The same pattern of association was observed with ischemic stroke with an inverse significant association for whites but not blacks (Table 4). However, hemorrhagic stroke did not demonstrate a significant relationship with eCRF, likely due to the small number of events across the eCRF tertiles.

The ROC curves were plotted among whites for ‘traditional risk factors only’ model and ‘traditional risk factors with eCRF’ model (Figure 1). The Area Under the Curve was higher for the ‘traditional risk factors with eCRF’ (c-statistic=0.6954; 95% CI 0.6754, 0.7155) compared to the model ‘traditional risk factors only’ (c-statistic=0.6892; 95% CI 0.6691, 0.7093). There was borderline difference in predictive power between the models (P -value = .05).

In addition, we found the association between eCRF and incident stroke was different between younger and older age groups among blacks and whites (Figure 2). Among whites, a significant inverse trend was observed across incremental eCRF tertiles in those who were 60 years or older, but not in their younger peers. However, among blacks, no association was observed across incremental eCRF tertiles in those who were younger or older. We also conducted a sensitivity analysis among those with vs. without history of heart disease and found the observed association between eCRF and incident stroke was not significantly different (results not shown).

Results for men and women did not differ (eTable 1 and eTable 2 in the Supplement). In the socioeconomic model that included an adjustment for race, there was an inverse association between higher levels of eCRF and incident stroke in both men and women. The fully-adjusted model showed that every 1-MET increase was associated with a 10% and 5% lower risk of total stroke in women and in men, respectively.

Discussion

In this large, population-based prospective bi-racial study of men and women, we found that non-exercise eCRF was a strong independent predictor of future stroke for whites but not for blacks, while results were similar for men and women. A 1-MET increase in eCRF for whites was associated with a 12% lower stroke risk but for blacks there was no benefit. A similar pattern of inverse association was also found for ischemic, but not hemorrhagic, stroke among whites. We believe this is the first population-based cohort study showing an inverse association between non-exercise eCRF and the risk of stroke in both sexes, and the first study to demonstrate a differential effect for blacks and whites for the association between eCRF and occurrence of stroke.

In the U.S., risk of having a first stroke is nearly twice as high for blacks than for whites.^{11, 54} Therefore, the primary prevention of stroke is particularly important in the black population. Additionally, many studies suggest that blacks have a lower level of CRF compared to whites,^{12–17} and also have a less significant increase in CRF following an exercise training program.⁵⁵ In our study, we too found that blacks had lower levels of eCRF. The mean level of eCRF in METs was 8.67 ± 2.06 among whites and was 7.96 ± 2.15 among blacks ($P < .001$). Most studies on PA or CRF and stroke were based on white cohorts, and very few studies included blacks.^{41, 56, 57} Over a 21-year follow-up period, the Atherosclerosis Risk in Communities (ARIC) study found a significant trend toward reduced incidence of stroke with increasing level of PA among blacks, but not in whites.⁵⁷ The earlier report from the REGARDS cohort by McDonnell and colleagues did not find a significant interaction between race and PA.⁴¹ These findings were opposite from the current study, where a significant inverse association between eCRF and stroke was demonstrated in whites, but not in blacks. Most blacks in ARIC were from one location, Jackson, Mississippi; whereas approximately 50% of the REGARDS blacks were from non-southern states. Therefore, our findings represent a broader representation of blacks on which to provide evidence of eCRF and stroke risk in blacks. Potential pathways for the observed inverse association between CRF and stroke risk among whites include its direct effect on carotid atheroma burden, arterial stiffness, neuroprotective factors, and endothelial dysfunction as well as its favorable impact on downstream development of stroke risk factors such as hypertension, DM, and hypercholesterolemia.^{58, 59} Higher BMI, lower socioeconomic levels, unfavorable lifestyle risk factors, and higher CVD risk factor burden appear to contribute substantially to the racial/ethnic differences in CRF¹⁵. These differences might partially explain the null findings among blacks, however, more research is needed to clarify the mechanisms between CRF and stroke risk and explain the different findings between whites and blacks.

The results of age-stratified analysis deserve further comment. Consistent with previous reports,^{10, 54} we also found that blacks had higher incidence of stroke than whites in younger participants (age < 60 years) (2.30% vs. 1.27%). Among older participants (age ≥ 60 years), stroke incidence was similar between blacks and whites (4.88% vs. 5.02%). The protective effect of higher levels of eCRF on stroke incidence was more pronounced in those 60 years or older in whites. Among older blacks, participants in the upper tertile had an inverse trend with stroke, but significance was not reached. Among younger blacks, the confidence

intervals were wide, which indicates the potentially low statistical power to conduct the age-stratified analysis in this subgroup.

One of the strengths of this study was its prospective nature with a large national population-based cohort of adult men and women, large proportions of both blacks and whites, which makes the results more generalizable to middle-aged and older blacks and whites across the U.S. Our ability to study stroke type in both men and women extended existing literature on the potential different effects of eCRF on hemorrhagic and ischemic stroke between men and women. We had data to adjust for numerous confounders, including participants' physical functioning information. Finally, the proposed method of eCRF is convenient, practical, and easy to implement in large-scale public health programs or clinical settings.

Limitations of this study must be acknowledged. First, data on non-exercise eCRF were available at baseline only. It is possible that eCRF might change during follow-up because components used to estimate CRF may change, which primarily would lead to an underestimation of the study association. In addition, baseline covariates that were adjusted in the models including those traditional cardiovascular risk factors and other downstream development of atrial fibrillation and congestive heart failure might also change. Future studies with repeated measures are warranted to better understand the association between eCRF and stroke. Second, we modified the PA components of the non-exercise equation³⁰ based on data available in REGARDS, which may have affected the eCRF values for some participants. Therefore, validation and refinement of the eCRF algorithm in other cohorts is needed to improve its application. Third, the non-exercise algorithm used in this study was developed from a cohort with majority of whites, therefore, it is not known if the validity of eCRF as a measure of CRF is valid in blacks, potentially contributing to the null findings among blacks. Fourth, the number of hemorrhagic strokes may have been too small to provide sufficient statistical power to find an association. The different biological mechanism hemorrhagic stroke played might also explain the null findings. Finally, the age-stratified analysis among blacks is likely lacking of statistical power to draw precise estimates.

Conclusions

In conclusion, the eCRF estimated from a simple non-exercise algorithm utilizing information routinely collected in clinical practice significantly predicted the risk for stroke in both men and women. The protective effect was only present for whites but not blacks. Although CRF is recognized as an important marker of cardiovascular health, it is currently the only major cardiovascular risk factor that is not routinely assessed in clinical practice.⁶⁰ Non-exercise eCRF might provide reasonably accurate estimates for initial CRF screening for stroke prevention. Considering the higher incidence of stroke among blacks and the potentially protective effect of higher level of eCRF in older blacks, greater efforts directed at the understanding and improving CRF in blacks are needed.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations List

AF	atrial fibrillation
BMI	body mass index
CHD	coronary heart disease
CI	confidence interval
CRF	cardiorespiratory fitness
CVD	cardiovascular disease
DM	diabetes mellitus
ECG	electrocardiography
eCRF	estimated cardiorespiratory fitness
HR	hazard ratio
LDL	low-density lipoprotein cholesterol
LVH	left ventricular hypertrophy
METs	metabolic equivalents
MI	myocardial infarction
PA	physical activity
REGARDS	The REasons for Geographic And Racial Differences in Stroke
RHR	resting heart rate
ROC	Receiver operating characteristic
SD	standard deviation
SF-12	12-item short form survey
TIA	transient ischemic attack

WC waist circumference

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Figure 1. Receiver Operating Characteristic (ROC) Curve comparing the predictive ability of the traditional cardiovascular risk factors (age, gender, education, region, systolic blood pressure, blood pressure-lowering medication, history of heart disease, diabetes, dyslipidemia, atrial fibrillation, left ventricular hypertrophy, and alcohol use) model to the traditional risk factors and estimated cardiorespiratory fitness (eCRF) model among whites.

Figure 2.

Multivariable*-adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) of incident stroke by tertiles of estimated cardiorespiratory fitness (eCRF) across age strata. *Adjusted for gender, education, region, systolic blood pressure, blood pressure-lowering medication, history of heart disease, diabetes, dyslipidemia, atrial fibrillation, and left ventricular hypertrophy, alcohol use, and physical functioning score. T1 (lower tertile) is the referent.

Table 1

Baseline characteristics of the study participants by blacks and whites in the Reasons for Geographic and Racial Difference in Stroke (REGARDS) study

Characteristic	Whites (n=14619)	Blacks (n=9543)	P Value ^a
Age, years	65.1 ±9.4	63.8 ±9.2	<.001
Women, %	49.7	62.6	<.001
Region, %			<.001
Belt	35.6	33.1	
Buckle	23.0	18.4	
Nonbelt	41.4	48.5	
Highest education, %			<.001
Less than HS	6.7	18.4	
HS graduate	24.2	27.6	
Some college	26.7	27.2	
College grad and above	42.3	26.8	
Alcohol use, %			<.001
Heavy	5.1	2.5	
Moderate	39.7	26.3	
None	55.2	71.2	
Smoke, %			<.001
Never	45.9	46.6	
Past	42.4	36.9	
Current	12.0	16.5	
Physical activity frequency, %			<.001
None	32.3	27.0	
1-3 times/week	36.7	37.4	
4 or more times/week	31.0	35.6	
Body mass index, kg/m ²	28.4 ±5.5	30.9 ±6.5	<.001
Waist circumference, cm	94.8 ±15.1	98.0 ±15.0	<.001
Resting heart rate, mbp	66 ±11	68 ±12	<.001
Estimated CRF, METs	8.7 ±2.1	8.0 ±2.1	<.001
Total cholesterol, mmol/dL	4.99 ±1.02	5.04 ±1.06	<.001
Fasting blood glucose, mmol/dL	5.57 ±1.61	6.07 ±2.34	<.001
Blood pressure, mmHg			
Systolic	125 ±16	131 ±17	<.001
Diastolic	75 ±9	78 ±10	<.001
Blood pressure-lowering medication, %	31.5	41.7	<.001
Heart disease, %	18.2	13.5	<.001
Atrial fibrillation, %	8.7	7.1	<.001
Left ventricular hypertrophy, %	6.5	14.5	<.001
Diabetes mellitus, %	14.8	28.5	<.001
Dyslipidemia, %	61.3	53.8	<.001

Characteristic	Whites (n=14619)	Blacks (n=9543)	P Value ^a
Physical function score ^b	48±10	46±10	<.001

METs, metabolic equivalents; HS, high school.

Data shown as Means ± SD unless specified otherwise.

^aPvalue based on t tests for mean differences and X² tests for differences in proportions.

^bAvailable among 23,520 participants.

Table 2

Baseline characteristics of the study participants across estimated cardiorespiratory fitness (eCRF) levels in the Reasons for Geographic and Racial Difference in Stroke (REGARDS) study

Characteristic	All (n=24162)	Tertile of eCRF			P Value ^a
		T1 (Lower) (n=8053)	T2 (Middle) (n=8053)	T3 (Upper) (n=8056)	
Age, years	64.6 ±9.3	67.5 ±10.8	64.5 ±8.7	61.8 ±7.3	<.001
Women, %	54.8	54.8	54.8	54.8	>.99
Blacks, %	39.5	47.2	40.2	31.1	<.001
Region, %					.02
Belt	34.6	33.6	35.7	34.5	
Buckle	21.2	20.1	21.5	21.1	
Nonbelt	44.2	46.3	42.9	43.4	
Highest education, %					<.001
Less than HS	11.4	15.4	11.2	7.4	
HS graduate	25.6	26.8	26.4	23.5	
Some college	26.9	27.8	27.0	26.0	
College grad and above	36.2	30.0	35.4	43.2	
Alcohol use, %					<.001
Heavy	4.1	2.8	3.8	5.6	
Moderate	34.4	29.0	34.3	39.9	
None	61.5	68.2	61.9	54.5	
Smoke, %					<.001
Never	46.2	45.1	44.7	48.8	
Past	40.1	41.5	40.8	37.9	
Current	13.7	13.4	14.6	13.3	
Physical activity frequency, %					<.001
None	32.8	45.8	31.8	20.8	
1-3 times/week	37.0	37.7	40.1	33.2	
4 or more times/week	30.2	16.4	28.1	46.0	
Body mass index, kg/m ²	29.4 ±6.0	34.5 ±6.4	28.8 ±3.6	24.9 ±2.9	<.001
Waist circumference, cm	96.1 ±15.1	108.0 ±14.6	95.2 ±10.1	85.0 ±10.2	<.001

Characteristic	Tertile of eCRF			P Value ^a
	All (n=24162)	T1 (Lower) (n=8053)	T2 (Middle) (n=8053)	T3 (Upper) (n=8053)
Resting heart rate, mbp	67 ±11	71 ±12	67 ±10	62 ±9
Estimated CRF, METs	8.4 ±2.1	6.6 ±1.6	8.5 ±1.5	10.1 ±1.7
Total cholesterol, mmol/dL	5.01 ±1.04	4.90 ±1.04	5.05 ±1.07	5.08 ±1.00
Fasting blood glucose, mmol/dL	5.77 ±1.95	6.26 ±2.32	5.77 ±1.93	5.27 ±1.35
Blood pressure, mmHg				
Systolic	127 ±16	132 ±16	127 ±16	123 ±16
Diastolic	77 ±10	78 ±10	77 ±9	75 ±9
Blood pressure-lowering medication, %	35.5	41.8	37.7	27.1
Heart disease, %	16.3	20.5	16.2	12.3
Atrial fibrillation, %	8.1	10.3	7.9	6.1
Left ventricular hypertrophy, %	9.6	13.0	10.2	5.7
Diabetes mellitus, %	20.2	32.7	19.1	8.9
Dyslipidemia, %	58.4	63.8	61.8	49.5
Physical function score ^b	47 ±10	43 ±11	48 ±10	50 ±8

METs, metabolic equivalents; HS, high school.

Data shown as Means ± SD unless specified otherwise.

^a P-value based on ANOVA tests for mean differences and χ^2 tests for differences in proportions.

^b Available among 23,520 participants.

Table 3

Association between estimated cardiorespiratory fitness (eCRF) and incident stroke across race, Reasons for Geographic and Racial Difference in Stroke (REGARDS) study

	Cases/No.	HR (95% CI)			
		Model 1	Model 2	Model 3	Model 4
Blacks					
Lower eCRF	151/3803	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
Middle eCRF	136/3237	0.91 (0.72–1.15)	0.92 (0.73–1.16)	1.03 (0.81–1.30)	1.07 (0.84–1.37)
Upper eCRF	90/2503	0.80 (0.62–1.04)	0.80 (0.61–1.04)	1.02 (0.77–1.34)	1.09 (0.82–1.45)
<i>P</i> -linear trend		.10	.09	.88	.54
Per 1-MET increase		0.93 (0.88–0.98)	0.94 (0.88–1.00)	1.00 (0.94–1.07)	1.02 (0.95–1.10)
Whites					
Lower eCRF	223/4250	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
Middle eCRF	203/4816	0.67 (0.55–0.81)	0.64 (0.53–0.78)	0.75 (0.61–0.90)	0.82 (0.67–1.00)
Upper eCRF	142/5553	0.38 (0.30–0.46)	0.37 (0.30–0.46)	0.48 (0.39–0.60)	0.54 (0.43–0.69)
<i>P</i> -linear trend		<.001	<.001	<.001	<.001
Per 1-MET increase		0.81 (0.78–0.84)	0.79 (0.75–0.83)	0.85 (0.80–0.89)	0.88 (0.83–0.93)

eCRF, estimated cardiorespiratory fitness; HR, Hazard ratio; CI, Confidence interval.

Model 1: Unadjusted;

Model 2: Adjusted for age, gender, education and region;

Model 3: Adjusted for variables in model 2 plus systolic blood pressure, blood pressure-lowering medication, history of heart disease, diabetes, dyslipidemia, atrial fibrillation, or left ventricular hypertrophy, and alcohol use;

Model 4: Adjusted for variables in model 3 plus physical functioning score.

Association between estimated cardiorespiratory fitness (eCRF) and subtypes of stroke by race, Reasons for Geographic and Racial Difference in Stroke (REGARDS) study

Table 4

Ischemic stroke/No.		Model 1	Model 2	Model 3	Model 4
Blacks					
Lower eCRF	138/3790	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
Middle eCRF	123/3224	0.90 (0.70-1.14)	0.90 (0.71-1.15)	1.01 (0.79-1.30)	1.07 (0.83-1.39)
Upper eCRF	76/2489	0.74 (0.56-0.98)	0.73 (0.55-0.97)	0.93 (0.69-1.24)	1.00 (0.74-1.37)
P linear trend		.04	.03	.65	.92
Per 1-MET increase		0.92 (0.87-0.97)	0.92 (0.86-0.98)	0.98 (0.91-1.05)	1.00 (0.92-1.07)
White					
Lower eCRF	202/4229	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
Middle eCRF	178/4791	0.64 (0.53-0.79)	0.62 (0.51-0.76)	0.72 (0.59-0.88)	0.79 (0.64-0.98)
Upper eCRF	125/5536	0.36 (0.29-0.45)	0.36 (0.29-0.45)	0.47 (0.37-0.59)	0.53 (0.41-0.67)
P linear trend		<.001	<.001	<.001	<.001
Per 1-MET increase		0.79 (0.76-0.83)	0.78 (0.74-0.82)	0.83 (0.79-0.88)	0.87 (0.82-0.92)
HR (95% CI)					
Hemorrhagic stroke/No.		Model 1	Model 2	Model 3	Model 4
Blacks					
Lower eCRF	14/3719	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
Middle eCRF	14/3159	1.02 (0.47-2.21)	1.07 (0.50-2.32)	1.21 (0.55-2.63)	1.05 (0.46-2.39)
Upper eCRF	13/2459	1.47 (0.69-3.12)	1.57 (0.73-3.38)	2.08 (0.94-4.58)	1.98 (0.87-4.52)
P linear trend		.33	.25	.08	.12
Per 1-MET increase		1.04 (0.90-1.21)	1.17 (0.95-1.45)	1.13 (0.97-1.32)	1.14 (0.97-1.34)
White					
Lower eCRF	21/4048	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
Middle eCRF	25/4638	0.89 (0.50-1.59)	0.89 (0.50-1.59)	0.99 (0.55-1.78)	1.06 (0.57-1.98)
Upper eCRF	17/5428	0.48 (0.26-0.92)	0.51 (0.27-0.97)	0.59 (0.30-1.16)	0.67 (0.33-1.36)
P linear trend	.02	.04	.13	.26	

Ischemic stroke/No.	Model 1	Model 2	Model 3	Model 4
Per 1-MET increase	0.93 (0.83-1.06)	0.89 (0.77-1.03)	0.93 (0.79-1.09)	0.97 (0.82-1.14)

eCRF, estimated cardiorespiratory fitness; HR, Hazard ratio; CI, Confidence interval.

Model 1: Unadjusted;

Model 2: Adjusted for age, gender, education and region;

Model 3: Adjusted for variables in model 2 plus systolic blood pressure, blood pressure-lowering medication, history of heart disease, diabetes, dyslipidemia, atrial fibrillation, or left ventricular hypertrophy, and alcohol use;

Model 4: Adjusted for variables in model 3 plus physical functioning score.