

Traditional Risk Factors as the Underlying Cause of Racial Disparities in Stroke

Lessons From the Half-Full (Empty?) Glass

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Background and Purpose—Black/white disparities in stroke incidence are well documented, but few studies have assessed the contributions to the disparity. Here we assess the contribution of “traditional” risk factors.

Methods—A total of 25 714 black and white men and women, aged ≥ 45 years and stroke-free at baseline, were followed for an average of 4.4 years to detect stroke. Mediation analysis using proportional hazards analysis assessed the contribution of traditional risk factors to racial disparities.

Results—At age 45 years, incident stroke risk was 2.90 (95% CI: 1.72–4.89) times more likely in blacks than in whites and 1.66 (95% CI: 1.34–2.07) times at age 65 years. Adjustment for risk factors attenuated these excesses by 40% and 45%, respectively, resulting in relative risks of 2.14 (95% CI: 1.25–3.67) and 1.35 (95% CI: 1.08–1.71). Approximately one half of this mediation is attributable to systolic blood pressure. Further adjustment for socioeconomic factors resulted in total mediation of 47% and 53% to relative risks of 2.01 (95% CI: 1.16–3.47) and 1.30 (1.03–1.65), respectively.

Conclusions—Between ages 45 to 65 years, approximately half of the racial disparity in stroke risk is attributable to traditional risk factors (primarily systolic blood pressure) and socioeconomic factors, suggesting a critical need to understand the disparity in the development of these traditional risk factors. Because half of the excess stroke risk in blacks is not attributable to traditional risk factors and socioeconomic factors, differential impact of risk factors, residual confounding, or nontraditional risk factors may also play a role. (*Stroke*. 2011;42:3369–3375.)

Key Words: stroke ■ risk factors ■ hypertension ■ diabetes mellitus ■ mediation analysis

The great success and horrid failure in reducing racial disparities in stroke mortality are shown in Figure 1A and 1B. The left panel was calculated from publically available data from the Centers for Disease Control and Prevention WONDER data system and shows the dramatic decline in stroke mortality between 1979 and 2006 by race and sex, with more than a 50% reduction in stroke mortality for both whites and blacks in only 27 years.¹ This striking decline in stroke (and heart disease) mortality was recognized as one of the 10 great public health achievements of the past century.² In 2000, the Healthy People 2010 statement, the guiding document for the US Department of Health and Human Services, set the lofty goal to eliminate health

disparities by the year 2010.³ The right panel was calculated from the information in the left panel and shows the 55% increase in the black-to-white stroke mortality disparity for men (from a 39% to 61% excess) and 26% increase for women (from a 31% to a 39%) over this period. Efforts to eliminate racial disparities in stroke mortality have been strikingly unsuccessful.

This racial disparity in stroke mortality has been recognized for decades⁴; however, there has been little advancement of the understanding of underlying causes. A higher prevalence of traditional risk factors (herein defined by inclusion in the Framingham stroke risk function⁵) in blacks likely contributes to these racial disparities in stroke risk. The

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The authors had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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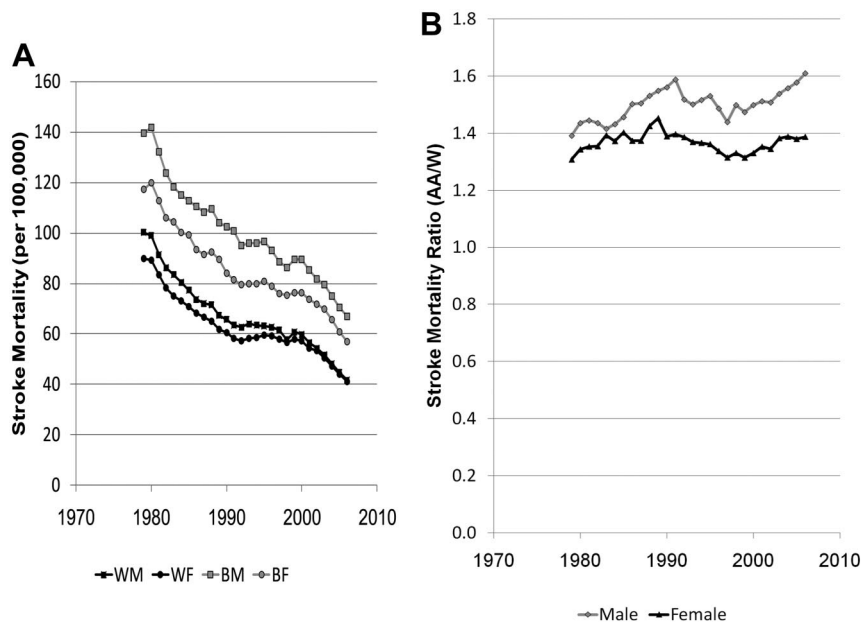


Figure 1. Age-adjusted (2000 standard) stroke mortality estimates for blacks and whites aged ≥ 45 years in the United States between 1979 and 2006 (A) and black:white stroke mortality ratio between 1979 and 2006 (B). Calculated from Centers for Disease Control and Prevention WONDER.¹ Age-adjusted stroke mortality and stroke black:white mortality ratio: 1979–2006. WM indicates white male; WF, white female; BM, black male; BF, black female.

American Heart Association notes that “the prevalence of hypertension in blacks in the United States is among the highest in the world,” and the prevalence of diabetes mellitus in blacks is 1.8 times greater than in whites.⁶ We have observed similar striking differences in the Reasons for Geographic and Racial Differences in Stroke (REGARDS) Study.⁷ In addition, the widely recognized black-white differences in socioeconomic status (SES) could affect stroke risk through multiple pathways.⁶

Differences in the magnitude of stroke mortality disparities across the age spectrum complicate interpretations, where the risk of death from stroke is 3 to 4 times higher for blacks than whites for ages 45 to 65 years, but there is a declining disparity with increasing age.^{8–11} Sixteen years ago, Giles et al¹² directly addressed the contribution of the higher prevalence of risk factors among blacks to the age-specific racial disparities in stroke incidence using the National Health and Nutrition Examination Survey follow-up data. They reported a 2.62 (95% CI: 1.23–5.57) black-to-white relative risk of incident stroke between ages 35 to 44 years, but adjustment for traditional risk factors attenuated this excess only 33% to 2.07 (95% CI: 0.97–4.42). Over age 64 years, the black-to-white excess was only 1.14 (95% CI: 0.90–1.46), but this was completely mediated to 0.82 (95% CI: 0.29–2.33) by risk factors. Herein we expand the observations of Giles et al¹² using data from the REGARDS Study.

Methods

REGARDS is a population-based longitudinal cohort study of black and white individuals aged ≥ 45 years. The sample was drawn from 1842 (59%) of the 3140 US counties and was recruited between 2003 and 2007 using a combination of mail and telephone contact (33% participation rate¹³). The study oversampled blacks and residents of the southeastern Stroke Belt (Alabama, Arkansas, Georgia, Louisiana, Mississippi, North Carolina, South Carolina, and Tennessee) and achieved a sample of 30 239, including 42% blacks and 56% residents of the Stroke Belt. Medical and risk factor histories were obtained by telephone interview and physical measurements done at an in-home visit (including phlebotomy, blood pressure, anthropom-

etry, and ECG). Incident stroke was ascertained using telephone surveillance every 6 months, along with retrieval and central physician adjudication of medical charts of suspected strokes. Because the racial disparities are an order of magnitude larger for blacks than other minority race/ethnic groups, REGARDS focused on the black and white disparity. Study design details¹⁴ and details of event identification and adjudication¹⁵ are available elsewhere.

In this article, we have limited risk factors potentially contributing to the racial disparity in stroke to the traditional risk factors as defined by inclusion in the Framingham stroke risk function.⁴ There are a wealth of “nontraditional” risk factors (ie, any risk factor not in the Framingham stroke risk function) that could be contributors, including body mass index, sleep apnea, markers of inflammation (C-reactive protein, etc), psychosocial factors (discrimination, etc), and many others. However, we have been guided by the Framingham risk factors in limiting factors considered and plan to assess the potential role of nontraditional risk factors in future articles. Likewise, there are many approaches to quantify the risk factors that were included, for example, smoking, which can be quantified as current/nonsmoker or as pack-years of exposure. Again, we have been guided to the approach of quantification by the approaches in Framingham and plan to assess potential additional contributions introduced by better quantification of risk factors in future articles.

The race of participants was determined by self-report. Systolic blood pressure was defined as the average of 2 seated measures taken after a 5-minute rest. Use of antihypertensive medications was defined by self-report. Diabetes mellitus was defined as fasting glucose of ≥ 126 mg/dL among the 87% of participants who complied with the request for an overnight fast, nonfasting glucose of ≥ 200 mg/dL among the 13% without an overnight fast, or self-reported use of medications for diabetes control. Atrial fibrillation was defined by self-report of a physician diagnosis or ECG evidence and left ventricular hypertrophy (LVH) by ECG. Current cigarette smoking was defined by self-report. History of heart disease was defined as a self-reported myocardial infarction, ECG evidence of myocardial infarction, or self-report of coronary artery bypass, angioplasty, or stent. Income (less than \$20 000, \$20 000 to \$34 000, \$35 000 to \$74 000, more than or equal to \$75 000, and refused response) and education (less than high school, high school graduate, some college, and college graduate) were defined by self-report. A stroke diagnosis was made by a committee of trained clinicians. Medical chart data including neuroimaging and other pertinent diagnostic reports were reviewed to confirm stroke type and possible etiology. Final adjudication was based on the World Health Organization’s definition of stroke.

Table 1. Description of Study Population by Race and by Race and by Those With and Without an Incident Stroke Outcome

Variable	White		Black	
	No Stroke	Stroke	No Stroke	Stroke
N	15215	246	10072	181
Demographic factors				
Age, mean±SD	65.1±9.4	71.0±8.0	63.8±9.2	67.8±8.9
Male, %	49.8	60.2	37.5	46.4
Risk factors				
Atrial fibrillation, %	8.6	19.9	7.2	8.3
Diabetes mellitus, %	14.9	20.7	29.2	32.6
Systolic blood pressure, mean±SD	125.0±16.5	131.9±17.6	130.4±17.1	139.0±18.3
Antihypertensive medications, %	41.6	54.5	61.8	71.8
Heart disease, %	17.8	36.2	13.6	23.2
Current smoking, %	12.1	18.3	16.6	24.3
Left ventricular hypertrophy, %	6.4	10.6	14.3	24.9
SES factors				
Education, %				
Less than high school	6.9	7.8	18.4	24.9
High school graduate	24.2	26.0	27.8	34.8
Some college	26.7	26.8	27.1	18.8
College graduate or more	42.2	39.4	26.7	21.5
Income, %				
Less than \$20 000	10.9	16.6	25.6	30.3
\$20 000 to \$34 000	22.3	28.5	26.3	29.3
\$35 000 to \$74 000	33.3	31.3	26.8	23.8
\$75 000 or more	21.7	11.0	9.6	4.4
Refused	11.8	12.6	11.7	12.2

SES indicates socioeconomic status; SD, standard deviation.

Proportional hazards analysis was used to estimate the black:white hazard ratio in a series of incremental models, first including demographic factors (age, race, age*race interaction, and sex), then additionally adjusting for risk factors (systolic blood pressure, antihypertensive medication use, diabetes mellitus, atrial fibrillation, LVH, heart disease, and cigarette smoking), and finally additionally adjusting for SES (indexed by income and education). The contribution of individual risk factors to the observed mediation of the racial disparity was assessed by the change in estimated black-to-white risk associated with its individual addition to the model. Multiple imputation techniques were used in the analysis to reduce the potential bias introduced through either failure to retrieve medical charts or from records remaining in the adjudication process at the time of analysis ($\approx 10\%$ each). Ten imputation data sets were used, with statistics calculated by the approach of Rubin.¹⁶ Additional details of the application of multiple imputation techniques in REGARDS are provided elsewhere.¹⁷

The focus of this article is the attenuation in the estimated black:white hazard ratio associated with adjustment for traditional risk factors and SES measures, estimated using the approach of MacKinnon et al.¹⁸ Briefly, the proportion of the excess risk attributable to these traditional risk factors was calculated by estimating the black:white hazard ratio before adjustment for the risk factors (HR_B) and after adjustment for the risk factors (HR_A). The amount of excess risk was calculated as the proportion of reduction of the black risk before and after adjustment for the risk factors, that

is $(HR_B - HR_A)/(HR_B - 1)$. Age (along with an interaction with race) was modeled as a continuous factor, and the attenuation of the black-to-white difference was estimated at arbitrary ages of 45, 55, 65, 75, and 85 years. The SE of the change in the hazard ratio was estimated by bootstrap methods with 100 replications.

Results

Follow-up was available on 29 612 (98%) of the 30 239 REGARDS participants. Of these, 1885 (6.0%) participants with prebaseline stroke were excluded, as were 2009 (7.0%) with ≥ 1 missing predictor variable and 4 participants ($<0.1\%$) with problematic follow-up times, resulting in a final analytic sample of 25 714.

At baseline, blacks were younger but had a higher use of antihypertensive medication, a higher prevalence of diabetes mellitus, LVH, and smoking, and lower SES than whites (Table 1). There were 427 stroke events detected over 4.4 years of follow-up, where among whites there were 203 ischemic strokes (83%), 31 hemorrhagic strokes (13%), and 12 nonspecific strokes (5%), whereas among blacks there were 152 ischemic strokes (84%), 22 hemorrhagic strokes (12%), and 7 nonspecific strokes (4%). Those with stroke

Table 2. Multivariable Association (Hazard Ratio With 95% Confidence Limits) of Demographic, Risk Factors, and Income With Subsequent Incident Stroke Events

Variable	All Stroke (n _{events} = 427)		
	Demographic Model	Risk Factor Model	SES Model
Demographic factors			
Age-by-race	See Figure 2	See Figure 2	See Figure 2
Male sex	1.22 (1.02–1.47)	1.12 (0.93–1.35)	1.20 (0.99–1.45)
Risk factors			
Atrial fibrillation		1.47 (1.14–1.89)	1.45 (1.13–1.87)
Diabetes mellitus		1.40 (1.13–1.72)	1.37 (1.11–1.69)
Systolic blood pressure (Δ10 mm Hg)		1.15 (1.09–1.21)	1.14 (1.08–1.20)
Use of antihypertensive medications		1.15 (0.93–1.42)	1.15 (0.93–1.42)
Heart disease		1.60 (1.29–1.98)	1.58 (1.27–1.97)
Current smoking		2.05 (1.64–2.57)	1.98 (1.58–2.48)
Left ventricular hypertrophy		1.41 (1.09–1.81)	1.40 (1.08–1.81)
SES factors			
Less than HS			1.00 (ref)
HS graduate			1.18 (0.86–1.60)
Some college			1.03 (0.74–1.44)
College graduate			1.07 (0.79–1.46)

Hazard ratios in each model (column) are after adjustment for other factors in the model. Note that the SES model also includes income, which was not significantly associated with stroke risk, and estimated hazard ratios were not provided.

SES indicates socioeconomic status.

were older, more likely to be black and male, and had adverse stroke risk factors and lower levels of SES than those remaining stroke free (Table 1).

The association of traditional risk factors with stroke is shown in Table 2. The relative risks of stroke in blacks compared with whites at different ages are provided in Figure 2 and Table 3 and ranged from 2.90 at age 45 years to 0.95 at age 85 years. There was a substantial attenuation of the black excess risk with the addition of risk factors and further attenuation with the addition of SES measures. The estimated mediation at specific ages, shown in Table 3, demonstrated that at ages ≤65 years (where the racial disparities in stroke risk are largest), the risk factors accounted for >40% of the excess stroke risk in blacks; the further addition of SES factors increased the mediation to ≈50%. The substantial attenuation associated with adjustment for risk factors was highly significant ($P<0.0001$), as was the attenuation with SES.

Table 4 provides the contribution of individual risk factors to the observed mediation of black-to-white risk in stroke. Systolic blood pressure proved to have the most powerful mediating effect, accounting for approximately one half of the combined risk factor effect. For example at age 45 years, the addition of systolic blood pressure to the demographic model reduced the hazard ratio for black race from 2.90 to 2.56, a reduction that was 45% as great as the joint effect of the addition of all 7 risk factors that mediated the hazard ratio to 2.14 $[(2.90-2.56)/(2.90-2.14)=0.45]$ (or 45%). Generally, the use of antihypertensive medications and diabetes mellitus

accounted for the next largest portion of the total mediation, accounting for approximately one third of the total mediating effect of all of the risk factors. At older ages, the higher prevalence of heart disease in whites implied that adjustment for this factor actually increased (ie, “negative mediation”) the black-to-white estimated risk.

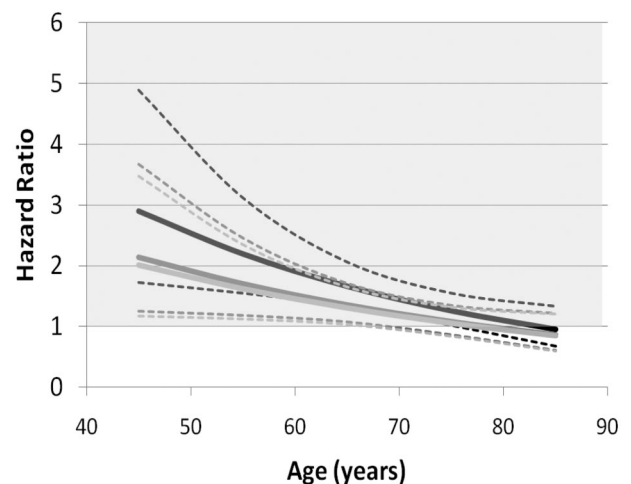


Figure 2. Estimated black:white hazard ratio as a function of age and covariate adjustment. Darkest lines show hazard ratio and 95% confidence limits after adjustment for sex; medium dark lines show hazard ratio and 95% confidence limits after further adjustment for Framingham stroke risk factors, and lightest lines show hazard ratio and 95% confidence limits after further adjustment for socioeconomic status (SES) factors. Mediation of black-white stroke risk by risk and SES factors.

Table 3. The Mediation by Stroke Risk Factors Is Described by the Estimated HR for All Stroke in Demographic Model and After Adjustment for Stroke Risk Factors and After Further Adjustment for Risk Factors Plus SES Measures

Outcome	Age	Mediation by Stroke Risk Factors			Effects After Further Adjustment for SES		
		HR Stroke in Blacks for Demographic Model (95% CI)	HR Stroke in Blacks for Risk Factor Model (95% CI)	% Decrease Comparing Risk Factor to Demographic Model (<i>P</i>)	HR Stroke in Blacks for Risk Factors+SES Model (95% CI)	% Decrease Comparing Risk Factors + SES to Demographic Model (<i>P</i>)	% Decrease Comparing SES to Risk Factor Model (<i>P</i>)
All Strokes	45	2.90 (1.72–4.89)	2.14 (1.25–3.67)	40 (<i>P</i> <0.0001)	2.01 (1.16–3.47)	47 (<i>P</i> <0.0001)	12 (<i>P</i> <0.0001)
	55	2.20 (1.55–3.12)	1.70 (1.18–2.45)	41 (<i>P</i> <0.0001)	1.62 (1.12–2.35)	48 (<i>P</i> <0.0001)	12 (<i>P</i> <0.0001)
	65	1.66 (1.34–2.07)	1.35 (1.08–1.71)	45 (<i>P</i> <0.0001)	1.30 (1.03–1.65)	53 (<i>P</i> <0.0001)	15 (<i>P</i> <0.0001)
	75	1.26 (1.02–1.55)	1.08 (0.86–1.34)	64 (<i>P</i> <0.0001)	1.05 (0.84–1.32)	76 (<i>P</i> <0.0001)	32 (<i>P</i> <0.0048)
	85	0.95 (0.68–1.34)	0.86 (0.60–1.21)	NA	0.85 (0.59–1.21)	NA	NA

Shown are the estimated decrease in the HR (eg, for all strokes at age 45 y, $[2.90-2.14]/[2.90-1.00] = 0.40$ or 40% decrease), and Wald *P* value where the SE of the decrease is estimated via bootstrapping techniques. The further mediation by adjustment for SES factors is shown by the hazard ratio after further adjustment for income and education and change in hazard ratio relative the demographic and risk factor model.

SES indicates socioeconomic status; NA, not applicable; HR, hazard ratio.

Discussion

Over the age range from 45 to 65 years where racial disparities in stroke incidence are largest, racial differences in risk factors and SES accounted for ≈50% of the black excess in stroke incidence, either a half-full (the part explained) or half-empty (the part failing to be explained) explanation. We observed a larger attenuation than the 33% mediation observed by Giles et al¹² ≈20 years ago. The risk factors appear to explain the majority of the mediation effect rather than SES indices, suggesting that a higher risk factor profile in blacks is a powerful and substantial contributor to the racial disparity in stroke risk (the half-full portion). Of the risk factors, hypertension (as indexed by systolic blood pressure and use of antihypertensive medications) and diabetes mellitus appear to be the largest contributors, accounting for one half and one third of the joint mediating effect of all of the

risk factors combined, respectively. That hypertension and diabetes mellitus are such powerful mediators is a product of both the large racial disparities in their prevalence (see Table 1) and their powerful association with stroke risk (see Table 2). However, the combination of risk factors and SES indices failed to account for half of the excess risk (the half-empty portion). These findings have substantial public health implications in considering elimination of racial disparities in stroke. Based on our findings, this goal will require efforts to reduce the impact of risk factors and SES indices and to advance the understanding of the contributors to the unexplained portion.

The factors considered here as mediators of the black excess stroke risk included the risk factors of diabetes mellitus, atrial fibrillation, LVH, and cigarette smoking (we note that systolic blood pressure is an actual level, hence it is

Table 4. Estimated Black:White Hazard Ratio All Stroke Outcome at Arbitrary Ages From the Demographic Model and From the Risk Factor Model and Black:White Hazard Ratio Associated With the Addition of Specific Risk Factors to the Demographic Model

Variable	Age, y									
	45		55		65		75		85	
	B:W Hazard Ratio	Mediation-Attributable to Factor, %	B:W Hazard Ratio	Mediation-Attributable to Factor, %	B:W Hazard Ratio	Mediation-Attributable to Factor, %	B:W Hazard Ratio	Mediation-Attributable to Factor, %	B:W Hazard Ratio	Mediation-Attributable to Factor, %
Demographic model	2.90		2.20		1.66		1.26		0.95	
All risk factor model	2.14		1.70		1.35		1.08		0.86	
Addition of single risk factors to the demographic model										
Atrial fibrillation	2.81	12	2.17	6	1.68	–6	1.30	–22	1.00	Undefined
Diabetes mellitus	2.73	22	2.05	30	1.54	39	1.16	56	0.87	Undefined
Systolic blood pressure	2.56	45	1.96	48	1.51	48	1.16	56	0.89	Undefined
Antihypertensive use	2.69	28	2.05	30	1.56	32	1.19	39	0.90	Undefined
Heart disease	2.76	18	2.16	8	1.70	–13	1.33	–39	1.04	Undefined
Current smoking	2.77	17	2.11	18	1.61	17	1.22	22	0.93	Undefined
LVH	2.82	11	2.12	16	1.60	19	1.20	33	0.91	Undefined

For example, at age 45 y, the B:W hazard ratio (HR) in the demographic model was 2.90, which was attenuated to 2.14 by adjustment for all of the risk factors; however, B:W HR for a model with the demographic factors plus atrial fibrillation was 2.81, which was 12% $[(2.90-2.81)/(2.90-2.14)]$ of the total mediation for that age.

B:W indicates black:white; HR, hazard ratio; LVH, left ventricular hypertrophy.

a measure of risk factor severity rather than prevalence). Hence, to reduce racial disparities in stroke we must prevent the development of the risk factors. As shown in Table 1, racial differences in the prevalence of these factors are striking, with blacks 20% more likely to be on antihypertensive medications and twice as likely to have diabetes mellitus and LVH. We reported previously that the 10-year predicted stroke risk based on these risk factors was also higher in blacks than in whites.⁷ It is likely that the higher prevalence rates of these risk factors are attributed to higher incidence rates for the risk factors (the alternative would be a longer life expectancy for those with the risk factors), and the most powerful approach to reducing racial disparities in stroke might be to focus efforts on reducing racial disparities in the incidence of these risk factors (and not the treatment of these factors). This “primordial prevention” of risk factors (or “protoprophylaxis,” as first called by Strasser¹⁹) requires knowledge of why there are disparities in the incidence of these risk factors. Unfortunately, knowledge regarding the contributors to racial differences in the incidence of risk factors is limited, and studies are urgently needed to allow appropriate interventions.

The findings of this study also suggest a need to improve the control of blood pressure in blacks. Others have shown that the odds of achieving blood pressure goals for treated black hypertensive patients is $\approx 40\%$ less than treated white hypertensive patients.^{20–24} Among the Framingham factors, this is the single risk factor affected by treatment of a prevalent condition.

Hence, reduction of racial disparities in stroke risk needs to focus on risk factor prevention. For example, prevalent diabetes mellitus is a lifelong diagnosis, and the models reported here include the presence and not the level of control of this condition. An effort to reduce disparities through these risk factors implies the prevention of the conditions. This potentially could be achieved through interventions on obesity or physical activity or other factors in the pathways of prevention. However, it is not clear whether there are other pathways leading to disparities in the development of these risk factors, a possibility that requires further research.

Considering the unexplained 50% of the racial disparity in stroke risk, there are several possible explanations that could individually or jointly be playing a role. First, the impact of risk factors could have a larger impact in blacks than whites. For example, given 2 hypertensive individuals, 1 black and 1 white, the same degree of elevated blood pressure could be associated with a larger increase in stroke risk for the black individual. That is, risk factors could be more “potent” in blacks than in whites. The possibility that risk factors may have a larger impact in blacks is not addressed herein, but can be evaluated in REGARDS with a larger number of events to permit assessment of statistical interactions. REGARDS was designed to accumulate a large number of stroke events, and as follow-up continues we will be able to assess the potential for a differential impact of risk factors in blacks.

Second, residual confounding from the studied risk factors could be contributing to the unexplained racial disparity in stroke. Framingham investigators used thoughtful approaches in the selection of risk factors as predictors of stroke risk; however, the quantification of the risk factor may not fully

capture all of the implied risk associated with the factor. For example, describing diabetes mellitus as present/absent fails to account for differences in either severity or duration of the disease. Describing smoking as current/not current may not be as sensitive a measure as pack-years of exposure. Being guided by the Framingham stroke risk function, we have described hypertension by systolic blood pressure and antihypertensive medication use. This fails to capture the severity or duration of the disease and also does not include other metrics of blood pressure assessment, such as pulse pressure. Many studies, including REGARDS, have extensive data collection instruments better quantifying the risk factors, but careful and hypothesis-driven modeling is needed to assess their additional contribution to stroke risk.

Third, it is possible that nontraditional risk factors not included in the Framingham risk score could be playing a role. These factors could include sleep apnea, elevated body mass index or physical inactivity, C-reactive protein, coagulation factors, stress, and depression. Future work in REGARDS will address these risk factors.

Finally (and almost certainly), part of the unexplained racial disparity in stroke is likely attributable to measurement error. As in other regression models, the proportional hazards model assumes that the predictor variables are measured with precision, a situation that is not the case. We attempted to minimize measurement error by using standardized approaches, including averaging of blood pressures and centralized training of field technicians.

This report has strengths and weaknesses. REGARDS is among the largest population-based longitudinal cohort studies in the United States and is accumulating a substantial number of physician-confirmed incident stroke events. The black and white participants are sampled from across the nation and come from a diverse spectrum of communities, and the findings are likely generalizable to the nation. We have also carefully designed and conducted the study to assess likely contributors to racial (and geographic) disparities in stroke. Both a strength and weakness of the study is the number of stroke events ($n=427$) that has been accumulated over a 4.4 year period. This number compares favorably with the number of events in other cohort studies, such as the 1136 incident strokes over 56 years of follow-up across all of the cohorts in the Framingham Study²⁵ (or 144 incident strokes over 8 years of follow-up from the original Framingham cohort²⁶), 577 over 15 years in the Atherosclerosis Risk in Communities Study,²⁷ 437 over 15 years in the Cardiovascular Health Study,²⁸ and the 660 over ≈ 12 years of follow-up in the National Health and Nutrition Examination Survey.¹² Although the number of strokes included in this analysis is comparable to these other studies and provides a solid foundation for the analyses reported herein, ongoing follow-up in REGARDS will accrue a larger number of stroke events for future analysis. A particular strength of REGARDS is the combination of a national sample with physician adjudication of events (in contrast to the reliance on discharge diagnoses of stroke events in the national sample of National Health and Nutrition Examination Survey). Our current findings focus on black/white disparities in stroke risk and fail to examine other racial/ethnic groups. The decision to

focus REGARDS on the black-white disparity in stroke risk was strategic, because this is both the largest disparity and a large minority group in the United States. The age-specific black/white disparities in stroke risk are in excess of 300% for ages 45 to 65 years, whereas disparities for other race/ethnic groups are a full order of magnitude smaller (eg, Hispanic-to-white disparities are $\approx 30\%$, Asian/Pacific Islander-to-white disparities are $<15\%$, and Native American-to-white disparities are $\approx 20\%$ ²⁹). Finally, herein we have reported the impact of risk factor adjustment on racial disparities in all types of stroke. These analyses have been repeated assessing the impact of risk factor adjustment on cerebral infarctions, providing similar results that have been omitted for brevity.

In conclusion, we demonstrate that, in the age range from 45 to 65 years (where the largest disparities exist), approximately half of the black-to-white disparities in stroke risk are attributable to traditional stroke risk factors and measures of SES. This gives rise to the urgent focus on strategies for primordial prevention of these risk factors, particularly hypertension and diabetes mellitus. Specifically, these findings suggest that half of the excess stroke incidence in blacks could be prevented if we could prevent blacks from having higher prevalence of risk factors. Although racial differences in SES significantly contributed to racial differences in stroke risk, the magnitude of the contribution was relatively small. These findings also suggest that the other half of the excess stroke risk in blacks is not attributable to risk factors and SES, implying that other pathways contribute to racial disparities in stroke risk. These could include a differential impact of risk factors in blacks residual confounding from the lack of a complete quantification of the traditional risk factors, and a role for nontraditional risk factors. Further work needs to focus on the relative contributions of these potential pathways.

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Disclosures

None.

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