Where to Focus Efforts to Reduce the Black–White Disparity in Stroke Mortality
Incidence Versus Case Fatality?

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Background and Purpose—At age 45 years, blacks have a stroke mortality ≈3× greater than their white counterparts, with a declining disparity at older ages. We assess whether this black–white disparity in stroke mortality is attributable to a black–white disparity in stroke incidence versus a disparity in case fatality.

Methods—We first assess if black–white differences in stroke mortality within 29681 participants in the Reasons for Geographic and Racial Differences in Stroke (REGARDS) cohort reflect national black–white differences in stroke mortality and then assess the degree to which black–white differences in stroke incidence or 30-day case fatality after stroke contribute to the disparities in stroke mortality.

Results—The pattern of stroke mortality within the study mirrors the national pattern, with the black-to-white hazard ratio of ≈4.0 at age 45 years decreasing to ≈1.0 at age 85 years. The pattern of black-to-white disparities in stroke incidence shows a similar pattern but no evidence of a corresponding disparity in stroke case fatality.

Conclusions—These findings show that the black–white differences in stroke mortality are largely driven by differences in stroke incidence, with case fatality playing at most a minor role. Therefore, to reduce the black–white disparity in stroke mortality, interventions need to focus on prevention of stroke in blacks. (Stroke. 2016;47:1893-1898. DOI: 10.1161/STROKEAHA.115.012631.)

Key Words: blacks ■ continental population groups ■ incidence ■ mortality ■ stroke
prevention of stroke in the black population. Conversely, if case fatality in blacks is the primary contributor, then the reduction of the black–white disparity must focus on efforts to reduce disparities in care of patients with stroke.

Remarkably, few studies have examined whether higher stroke incidence versus high case fatality in blacks is the primary contributor to the higher stroke mortality in blacks. The Greater Cincinnati/Northern Kentucky Stroke Study used stroke surveillance approaches and showed an age-specific pattern of black–white differences in stroke incidence in 1999 in the Cincinnati region that is quite similar to the national age-specific pattern for black–white differences in mortality, with stroke mortality 2.6× greater in blacks than in whites at age 45 to 54 years, but monotonically decreasing to 0.8× for ages 85+ years. The Greater Cincinnati/Northern Kentucky Stroke Study also showed that stroke case fatality was 24% lower in blacks than in whites. Likewise, data from the National Hospital Discharge Survey showed consistently higher discharge rates for stroke per 1000 population for blacks than whites but generally lower in-hospital mortality after stroke for blacks than whites. The pattern of a declining black–white disparity in stroke incidence has been previously confirmed in the REGARDS cohort; however, case fatality data have not been reported from the REGARDS cohort. Collectively, these data suggest that the key to reducing the black disparity in stroke mortality is through risk factor prevention or improved risk factor control to prevent strokes in blacks rather than improved care of blacks once stroke has occurred. The goal of the current report is to confirm the findings in a national cohort of black and white participants.

Methods

The REGARDS study is a longitudinal cohort study of 30239 black and white participants aged 45+ years. The cohort was recruited from the 48 contiguous states in the United States between 2003 and 2007 through a combination of mail and telephone contacts. An interview assessing the risk profile was conducted by telephone, and an in-home visit was subsequently performed for assessment of blood pressure, height, waist circumference, weight, and biological specimen collection. The cohort has been followed up at 6-month intervals by telephone for surveillance of potential strokes, with medical records for suspected stroke events retrieved and adjudicated by a physician panel. Details of the study are available elsewhere. All participants provided written informed consent, and the study methods were approved by institutional review boards at all participating entities.

The excess stroke mortality in blacks has been documented in the Vital Statistics Systems from the National Center for Health Statistics, with mortality ≈3× higher in blacks than in whites at age 45 years but a declining disparity at older ages. The first goal of this article was to validate data from the REGARDS study by confirming whether the black–white pattern of stroke deaths in the REGARDS study reflects these national data. Incident fatal stroke was defined as a death within 30 days of a physician-adjudicated stroke event and as such represents the product of both incidence and case fatality. Because the disparity in National Center for Health Statistics mortality includes both initial and recurrent stroke, we included the risk of incident fatal strokes among participants who are stroke free at baseline and those who are self-reporting previous stroke at baseline. The potential of a black–white disparity in fatal stroke was assessed using proportional hazards analysis, with factors for race, age, race-by-age interaction, and sex.

We then investigated whether the (potential) disparity in fatal strokes was attributable to:

- Black–white disparities in stroke incidence (either fatal or non-fatal) during follow-up using an analytic approach identical to that described above for incident fatal stroke.
- The black–white difference in case fatality was assessed in analysis restricted to those participants with a documented stroke during follow-up. Case fatality was defined by the proportion of these participants dying within 30 days of an adjudicated stroke event. The black–white difference in case fatality was assessed using logistic regression, with terms for race, age, race-by-age interaction, and sex.

The potential age-by-race interaction was tested in all models with an a priori α=0.10.

Results

Of the 30239 REGARDS participants, follow-up was available on 29682 (98%). A description of the study population is provided in Table 1. The white participants were slightly older, were more likely to be men, were less likely to have low income or education, and generally have fewer stroke risk factors. During an average follow-up of 6.8±2.7 years, there were 1168 strokes; of which, 242 were fatal.

Analysis of Time to Incident Fatal Stroke

The interaction between race and age was significant (P=0.0042), and as such, the black–white differences in the time to fatal stroke are described by age.

When age is categorized in decades, there is a monotonically decreasing black-to-white stroke mortality ratio by age (Figure 2A). There were only 5 fatal strokes in the youngest age stratum (4 in black and 1 in white participants), resulting...
in a wide confidence interval. For the older age strata, the black-to-white mortality ratio approaches 1.0 (and is nonsignificantly <1.0 for ages 85+ years).

The monotonically decreasing black-to-white mortality ratios by decade support the analysis with age as a continuous variable (Figure 2B, where the black-to-white mortality ratio decreases from ≈4.0 at age 45 years, down to 1.0 at age 85 years). This pattern generally reflects the black-to-white mortality ratio from Vital Statistics.

Analysis of Time to Incident Stroke (Fatal or Nonfatal)
For the time to any stroke, the interaction between race and age was significant (P=0.0003), and as such, the black–white differences in the time to any stroke are described by age. Figure 3A shows the black-to-white stroke incidence ratio with age categorized by decade, showing a monotonically decreasing black-to-white ratio that is ≈3.0 at age 45 to 54 years but decreases to ≈1.0 by age 75 to 84 years. This monotonically decreasing black-to-white incidence ratio supports the analysis of the incidence ratio with age as a continuous variable (Figure 3B), where the black-to-white incidence ratio decreases from ≈2.5 at age 45 years, down to 1.0 at age 85 years. This pattern generally reflects the black-to-white mortality ratio from Vital Statistics.

Analysis of Case Fatality
The age-specific number of fatal strokes and total strokes, with sex-adjusted black-to-white odds ratios, is shown in Table 2. There was no evidence of any 2-way interactions between age, race, and sex (P>0.10), and as such, only main effects were assessed. In multivariable analysis, the odds of a stroke being fatal increased by 61% with each decade (odds ratio, 1.61; 95% confidence interval, 1.35–1.91); but there was no evidence that either race (odds ratio, 1.20; 95% confidence interval, 0.89–1.62) or sex (odds ratio, 1.02; 95% confidence interval, 0.76–1.36) was associated with case fatality.

Discussion
These data support the previous findings that the increased stroke mortality among middle-aged (45–65 years) blacks is attributable to black–white differences in stroke incidence and that black–white differences in case fatality is at most a minor contributor. The finding that case fatality is lower in blacks than in whites is supported by recent reports from Get With The Guidelines hospitals, where after adjustment for patient and hospital characteristics, the odds of in-hospital death in blacks was 0.90-fold (95% confidence interval, 0.85–0.95) that of whites. Hence, reducing the black-to-white disparity in stroke mortality will require further understanding and interventions to reduce the higher incidence of stroke in blacks. Although it is appropriate to work to reduce the disparities in stroke care, this will be unlikely to substantially reduce the disparity in stroke mortality. The key will be interventions focused on approaches to risk factor prevention and management, with primary care physicians and public health programs playing a key role.

The REGARDS study has already provided some insights to the black–white disparity in stroke incidence, but much work remains. Previous reports from the REGARDS study

Table 1. Description of the Study Population by Race

<table>
<thead>
<tr>
<th></th>
<th>Black</th>
<th>White</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>12212</td>
<td>17470</td>
</tr>
<tr>
<td>Age, mean±SD</td>
<td>64±9</td>
<td>65±9</td>
</tr>
<tr>
<td>Men, %</td>
<td>38</td>
<td>50</td>
</tr>
<tr>
<td>Income &lt;$35K, %</td>
<td>61</td>
<td>39</td>
</tr>
<tr>
<td>High school or less, %</td>
<td>48</td>
<td>32</td>
</tr>
<tr>
<td>Previous stroke, %</td>
<td>8</td>
<td>5</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>71</td>
<td>51</td>
</tr>
<tr>
<td>Diabetes mellitus, %</td>
<td>31</td>
<td>16</td>
</tr>
<tr>
<td>Current smoking, %</td>
<td>17</td>
<td>13</td>
</tr>
<tr>
<td>Atrial fibrillation, %</td>
<td>8</td>
<td>10</td>
</tr>
<tr>
<td>Left ventricular hypertrophy, %</td>
<td>15</td>
<td>6</td>
</tr>
<tr>
<td>Heart disease, %</td>
<td>16</td>
<td>20</td>
</tr>
</tbody>
</table>

Figure 2. A and B. Black-to-white (B:W) hazard ratio (with 95% confidence limits) for fatal stroke (mortality analysis) after adjustment for sex. A. Hazard ratio from a model with age as a categorical variable. B. Hazard ratio from a model with age as a continuous variable.
have shown that ≈40% of the black–white incidence disparity between the ages of 45 to 65 years can be attributed to prevalence of traditional risk factors (defined by the Framingham Stroke Risk Function11), particularly treated hypertension and prevalent diabetes mellitus, both of which are substantially higher in the black population than in the white population.12 Eliminating the disparity in stroke risk factors will be challenging; however, failure implies the continued persistence of the disparity not only in risk factors but also in stroke incidence and mortality.

Although the prevalence in stroke risk factors accounts for ≈40% of the disparity in stroke incidence, we have previously suggested12 that the remaining 60% of the disparity could be associated with:

1. Awareness, treatment and control of risk factors: data from both National Health and Nutrition Examination Survey and REGARDS have shown that although awareness and treatment for hypertension are higher in the black population than in whites, the likelihood of adequate control is much lower.13,14 Hence, hypertension is a triple threat as a contributor to the black–white disparity in stroke incidence as it has a higher prevalence, is less likely to be controlled, and the harm of lack of control has more potent effect. It has been suggested that the disparities in hypertension control may be attributable to differences in social conditions.15 In contrast, for dyslipidemia, blacks are less likely to be aware, less likely to be treated, and less likely to be controlled.16,17 Likewise, blacks have poorer control of diabetes mellitus19 and are less likely to be aware of or treated for atrial fibrillation.20 Interventions targeted to address prevention and control of risk factors in the stroke-free population are needed.

2. Risk factors having a differential effect by race, with a more potent effect in the black population: for example, we have previously shown that the effect of high blood pressure is larger in the black than in white population, where after multivariable adjustment for other risk factors, a 10-mmHg higher blood pressure is associated with an 8% increase risk of stroke in whites but a 24% increase risk in blacks.21 This apparent differential susceptibility could be playing a major role as there were no disparities in stroke incidence in subjects with well-controlled (<120 mmHg) systolic blood pressure.

3. Disparities in nontraditional risk factors: beyond the Framingham stroke risk factors, there are a plethora of risk factors that are both shown to be related to stroke and where blacks have a disadvantage in the prevalence or severity.22,23 Among the risk factors declared as well documented in the primary prevention guidelines, blacks have a disadvantage in prevalence or severity for physical inactivity,24,25 diet,26 and obesity.27 In addition, there are numerous less-well documented risk factors, such as psychosocial factors, including depressive symptoms, anger, hostility, and discrimination that are likely related to stroke for which blacks are at a disadvantage for prevalence or severity.28 Blacks are also at a disadvantage for environmental and neighborhood exposures that are related to stroke risk, including an alarmingly disproportionate number living in poverty, one of the strongest risk factors for stroke and other cardiovascular disease outcomes.29,30 Much work remains to continue to

Table 2. Number of Deaths and Number of Stroke Events (With Percentage) for Black and White Participants by Age Strata and the Sex-Adjusted Odds Ratio (With 95% CI)

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Black, n (%)</th>
<th>White, n (%)</th>
<th>Sex-adjusted black–white odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>45–54, y</td>
<td>4/24 (16.7)</td>
<td>1/11 (9.1)</td>
<td>1.99 (0.20–20.28)</td>
</tr>
<tr>
<td>55–64, y</td>
<td>29/151 (19.2)</td>
<td>19/134 (14.2)</td>
<td>1.44 (0.76–2.71)</td>
</tr>
<tr>
<td>65–74, y</td>
<td>35/214 (16.4)</td>
<td>40/255 (15.7)</td>
<td>1.05 (0.64–1.73)</td>
</tr>
<tr>
<td>75–84, y</td>
<td>35/113 (31.0)</td>
<td>58/225 (25.8)</td>
<td>1.29 (0.78–2.13)</td>
</tr>
<tr>
<td>85+, y</td>
<td>5/13 (38.5)</td>
<td>15/28 (53.6)</td>
<td>0.54 (0.14–2.07)</td>
</tr>
</tbody>
</table>

CI indicates confidence interval.
document nontraditional risk factors that are related to stroke where blacks are at a disadvantage for prevalence or severity of the risk factor, so that interventions and policies can address them.

4. Measurement error and residual confounding: all regression models (including both the proportional hazards and logistic models used here) assume that the predictor variables are measured with precision. For the predictor variables in this analysis (age, race, and sex), it is reasonably safe to assume that this is not a major issue. However, in other analyses where predictor variables are measured with a larger error, this could be a greater concern and lead to an underestimation of the proportion of the excess explained.

Despite the dramatic decline in stroke deaths for both blacks and whites, the black–white disparity in stroke mortality persists (or may be growing). Although some inroads have been made to understand the contributors to the higher risk of stroke incidence in blacks, there is much work remaining. The challenge for the REGARDS study and other epidemiological cohorts is to intensify the focus of investigations to identify the contributors, so that clinical trials can be developed to test the targeting of interventions to reduce this black–white stroke mortality disparity.

On the surface, it would seem that disparities in secondary stroke prevention could also play a role. Of the estimated 795 000 stroke events in the United States, ≈185 000 (23%) are recurrent events. Although much less is known about the role of risk factors and the black–white disparities for secondary stroke events, data from the REGARDS study have shown no black–white differences in the risk of recurrent stroke, and as such, it is relatively unlikely that secondary stroke prevention is a pathway to reducing the black–white disparity in stroke mortality.

It is clear that there are substantial black–white differences in care after stroke, and we explicitly do not want to minimize the importance of addressing disparities in stroke care. However, case fatality after stroke did not differ between blacks and whites in either this REGARDS analysis or the previous Greater Cincinnati/Northern Kentucky Stroke Study, suggesting that these disparities in care are unlikely to be contributors to the disparities in stroke mortality. This is not to say that it is unimportant to reduce documented black–white disparities in care, where after adjustment for patient and hospital characteristics, black stroke patients were less likely than whites to receive intravenous tissue-type plasminogen activator, be discharged on antithrombotics, be provided the use of anticoagulation for atrial fibrillation, to have low-density lipoproteins treated to 100 mg/dL, and to receive smoking cessation counseling; it is only that these disparities do not seem to be major contributors to the black–white disparity in stroke mortality. In addition, the distinction between prestroke and poststroke is not always crisp, and many of our study participants could have some level of cerebrovascular disease that could affect memory and functional assessment before an acute stroke event.

Conclusions
The substantial black–white differences in stroke mortality between the ages of 45 and 65 years are largely driven by black–white disparities in stroke incidence. This observation should bring attention to the need to focus efforts to reduce the black–white disparity on contributors to higher stroke incidence in blacks. A substantial proportion of the excess risk of incident stroke in blacks is attributable to a higher prevalence of traditional risk factors in blacks, and we need to go further upstream to make inroads to reduce this pathway (ie, why do blacks have a higher prevalence of hypertension and diabetes mellitus). However, there are many other pathways, including differential susceptibility to risk factors, disparities in the control and treatment of risk factors, socioeconomic inequities, and novel or emerging risk factors, where blacks have a disadvantage. We are at the early phase of processes to better understand these alternative pathways that potentially contribute to the black–white disparity in stroke incidence, and we need to redouble our efforts to the investigations of these pathways.

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Disclosures
None.

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