Blood Pressure and Racial Disparities in Stroke

The REasons for Geographic and Racial Differences in Stroke (REGARDS) Study

George Howard
for the REGARDS Investigators
School of Public Health
University of Alabama at Birmingham

Relative Risk of Stroke Mortality by Age and Ethnicity: 2006

(white reference)

Costs of “extra” strokes among African Americans

- Between 1999 and 2007 there was an annual average of 6,075 “extra” deaths in African Americans
- Projected to be associated with 24,299 “extra” stroke events
- Cost of stroke is $140,000
- Just the excess in stroke among blacks is associated with $3.4B in annual public health burden
- However, since stroke occurs at younger ages this is very conservative estimate
REGARDS
Overview of a Novel Study Design to Meet Study Needs

- Central participant recruitment using mail and telephone
- Central computer-assisted telephone interview
- In-home evaluation for physical, venipuncture and ECG:
  - EMSI: Examination Management Services, Inc
- Central facilities
  - Laboratory and repository for serum and urine samples: University of Vermont
  - ECG Reading Center: Wake Forest University
- Central follow-up for detection of suspected stroke events (+ MI, VTE and fractures; plus cognitive change)
- Physician adjudication of stroke events

REasons for Geographic And Racial Differences in Stroke (REGARDS)
Study Population

- Longitudinal population-based cohort of 30,239 volunteers age 45 and older
- Simple random sampling with geographic representation
  - 21% from the buckle of the stroke belt (goal was 20%)
  - 35% from the stroke belt (goal was 30%)
  - 44% from the rest of the contiguous US (goal 50%)
- Racial representation: 42% African American / 58% white (goal was 50/50%)
- Sex representation: 45% male / 55% female (goal was 50/50%)

REGARDS Participants
Methods

• Of the 30,239 REGARDS participants
  – 25,727 (85%) stroke-free at baseline and with full data
  – 489 physician-adjudicated incident stroke events over 4.5 year average follow-up
• Analysis:
  – Estimated black-to-white incident stroke risk
  – Assessed the proportion of risk attributable to traditional risk factors and SES

Potential for Mediation?

<table>
<thead>
<tr>
<th>Demographic Factors</th>
<th>Race</th>
<th>Incident Stroke During Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>White</td>
<td>Black</td>
</tr>
<tr>
<td></td>
<td>13636</td>
<td>10254</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Race</th>
<th>Incident Stroke During Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>White</td>
<td>Black</td>
</tr>
<tr>
<td>Age (mean ± SD)</td>
<td>65.2 ± 9.4</td>
<td>63.8 ± 9.2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SES Factors</th>
<th>Race</th>
<th>Incident Stroke During Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Less than High School</td>
<td>High School Graduate</td>
</tr>
<tr>
<td>Education (%)</td>
<td>6.9</td>
<td>18.3</td>
</tr>
<tr>
<td>Income (%)</td>
<td>Less than $20K</td>
<td>$20K - $34K</td>
</tr>
<tr>
<td></td>
<td>11.2</td>
<td>25.5</td>
</tr>
</tbody>
</table>

Black-to-White Stroke Incidence Rate Ratio (by Age)

(Preliminary REGARDS data – not for publication or presentation)
Blood Pressure and Racial Disparities in Stroke

George Howard, MD

**Black-to-White Stroke Incidence Rate Ratio (by Age)**

(Preliminary REGARDS data – not for publication or presentation)

---

So what actually happened with adjustment for just risk factors?

So do the risk factors and SES explain the racial disparities in stroke?

---

... and how about further adjustment for SES?

---

**Black-to-White Stroke Incidence Rate Ratio (by Age)**

(Preliminary REGARDS data – not for publication or presentation)

---

**Black-to-White Stroke Incidence Rate Ratio (by Age)**

(Preliminary REGARDS data – not for publication or presentation)
### Mediation of Racial Disparities by Risk Factors and SES at Specific Ages

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Age</th>
<th>HR for Demographic Model (95% CI)</th>
<th>% Decrease from Demographic Model</th>
<th>% Decrease Relative to Demographic Model</th>
<th>HR for Risk Factor Model (95% CI)</th>
<th>% Decrease from Risk Factor Model</th>
<th>% Decrease Relative to Risk Factor Model</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Strokes</td>
<td>45</td>
<td>2.90 (1.72–4.89)</td>
<td>40.3% (p &lt; 0.0001)</td>
<td></td>
<td>2.14 (1.25–3.64)</td>
<td>47.3% (p &lt; 0.0001)</td>
<td>47.3% (p &lt; 0.0001)</td>
</tr>
<tr>
<td>All Strokes</td>
<td>55</td>
<td>2.20 (1.55–3.12)</td>
<td>40.9% (p &lt; 0.0001)</td>
<td></td>
<td>1.71 (1.19–2.45)</td>
<td>48.1% (p &lt; 0.0001)</td>
<td>48.1% (p &lt; 0.0001)</td>
</tr>
<tr>
<td>All Strokes</td>
<td>65</td>
<td>1.66 (1.34–2.07)</td>
<td>44.9% (p &lt; 0.0001)</td>
<td></td>
<td>1.37 (1.09–1.72)</td>
<td>52.9% (p &lt; 0.0001)</td>
<td>52.9% (p &lt; 0.0001)</td>
</tr>
<tr>
<td>All Strokes</td>
<td>75</td>
<td>1.26 (1.02–1.55)</td>
<td>64.4% (p &lt; 0.0001)</td>
<td></td>
<td>1.09 (0.88–1.36)</td>
<td>75.9% (p &lt; 0.0001)</td>
<td>75.9% (p &lt; 0.0001)</td>
</tr>
<tr>
<td>All Strokes</td>
<td>85</td>
<td>0.95 (0.68–1.34)</td>
<td>N/A</td>
<td></td>
<td>0.87 (0.62–1.24)</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

### Specific Risk Factors Contributing to the Mediation

<table>
<thead>
<tr>
<th>(Preliminary REGARDS data -- not for publication or presentation)</th>
<th>Age</th>
</tr>
</thead>
<tbody>
<tr>
<td>45</td>
<td>55</td>
</tr>
<tr>
<td>Demographic Model</td>
<td>2.20</td>
</tr>
<tr>
<td>Atrial Fibrillation</td>
<td>2.97</td>
</tr>
<tr>
<td>Diabetes</td>
<td>2.77</td>
</tr>
<tr>
<td>Hypertension</td>
<td>2.55</td>
</tr>
<tr>
<td>Heart Disease</td>
<td>2.78</td>
</tr>
<tr>
<td>Current Smoking</td>
<td>2.78</td>
</tr>
<tr>
<td>LVH</td>
<td>2.77</td>
</tr>
</tbody>
</table>

### Approaches to reduce racial disparities in stroke?

- **So what can be done to address the half-full portion?**
  - For risk factors (for example, hypertension and diabetes) we are examining prevalent disease (present/absent) ... not effectiveness of treatment
  - This implies that risk factor treatment is not the key ... but risk factor prevention
  - Suggesting that focus of “racial disparities in stroke” research should shift to “racial disparities in risk factor prevention” research

- ... and what could be causing the half empty portion?
  - **Differential susceptibility to risk factors?**
  - **Residual confounding?**
  - Impact of “non-traditional” risk factors?
  - Measurement error?
Blood Pressure and Racial Disparities in Stroke

George Howard, MD

Differential impact of BP?

Adjusted for age, race, age x race, sex and antihypertensive use

Hazard Ratio (10 mmHg)

Differential impact of BP?

Adjusted for age, race, sex and antihypertensive use

\[ p_{\text{interaction}} = 0.016 \]

Differential impact of BP?

Adjusted for age, race, age x race, sex and antihypertensive use + Adjustments for risk factors

\[ p_{\text{interaction}} = 0.016 \]

\[ p_{\text{interaction}} = 0.049 \]
Implications of Differential Susceptibility?

- Many interactions between race, age, and SBP
- Consider black-white stroke risk differences within strata by age and SBP
  - Age: <65, 65-74, 75+
  - SBP:
    - Normotensive (<120 mmHg)
    - Prehypertension (120 – 139 mmHg)
    - Stage 1 hypertension (140 – 159 mmHg)
    - Stage 2 hypertension (160+ mmHg)
- Black stroke risk is at young ages (< 65 years mainly)
- Remember the excess black stroke risk is at young ages (< 65 years mainly)

![Black-white stroke risk within age-SBP strata](image)

**Black-white stroke risk in young (<65) normotensive (< 120 mmHg)**

<table>
<thead>
<tr>
<th>Age 75+</th>
<th>Age 65-74</th>
<th>Age &lt;65</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR</td>
<td>HR</td>
<td>HR</td>
</tr>
<tr>
<td>White</td>
<td>Black</td>
<td></td>
</tr>
<tr>
<td>0.81</td>
<td>1.09</td>
<td>0.89</td>
</tr>
<tr>
<td>1.39</td>
<td>1.26</td>
<td>1.15</td>
</tr>
<tr>
<td>3.71</td>
<td>1.51</td>
<td>1.20</td>
</tr>
</tbody>
</table>

* All hazard ratios are risk factor adjusted

Suggests differential susceptibility could be a key to racial disparities in stroke

Most importantly... it provides very addressable targets for intervention
Blood Pressure and Racial Disparities in Stroke
George Howard, MD

... so SBP and Racial Disparities in Stroke

- Strike 1: African Americans are more likely to be hypertensive
  - 51% of whites versus 71% of AAs in REGARDS
  - Everyone knows this
- Strike 2: African Americans are more likely to know they are hypertensive, more likely to be treated, but less likely to be controlled
  - B/W odds ratio for control = 0.70
  - Fewer people know this
- Strike 3: Once blood pressure is not controlled, it is much worse for AAs than whites
  - Twice as bad!
  - Shown here for the first time ... we think this is real news

Conclusions and Future?

- On the cusp (actually already beginning) to provide insights not about if there are disparities, but why blacks (and southerners) have higher stroke mortality
  - Shown herein
    - Shown that “traditional” risk factors account for about half the excess in incidence
    - Of the half that is explained, SBP accounts for about half the mediation, and diabetes accounts for about a quarter (other risk factors smaller effects)
    - That differential susceptibility to risk factors (particularly SBP) could be playing a truly major role
  - Well positioned and work is underway to address factors accounting for the unexplained excess
  - Similar work is underway on geographic disparities
- Study has an “open door policy” to potential authors and new investigators

REGARDS Functional Units