Stroke Update:
Prevention, Disparities &
New Advances in Care

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Chief Science Officer, Association of Black Cardiologists, Inc.
The Cost of Stroke

- The estimated direct and indirect cost of stroke is $73.7 billion in 2010.

- The mean lifetime cost of ischemic stroke is about $140,048 in America.

Stroke 101. Available at: http://www.stroke.org
Stroke Facts

• A leading cause of death in the US

• 795,000 Americans suffer strokes each year

• 137,000 deaths each year
  - From 1996 to 2006, the stroke death rate fell 33.5% and number of deaths fell by 18%

• 6,400,000 stroke survivors

Stroke 101. Available at: http://www.stroke.org
African Americans (AA) & Stroke

- Incidence is nearly double that of Caucasians
- AA suffer more extensive physical impairments
- Twice as likely to die from stroke than Caucasians
- High incidence of risk factors for stroke
  - Hypertension
  - Diabetes
  - Obesity
  - Smoking
  - Sickle cell anemia

Available at: http://www.stroke.org
Annual Rate of All First-ever Strokes by Age, Sex and Race (GCNKSS: 1999)

Source: GCNKSS unpublished data.

Note: rates for ages 45-54 for black men & women & for black men 75 and over, are considered unreliable.
Annual Age-Adjusted Incidence of 1st-ever Stroke, By Race: Inpatient Plus Out-of-hospital Ascertainment

Women & Stroke

- Stroke kills more than twice as many American women every year as breast cancer.
- More women than men die from stroke and risk is higher for women due to higher life expectancy.
- Women suffer greater disability after stroke than men.
- Women ages 45 to 54 experiencing a stroke surge, mainly due to increased risk factors and lack of prevention knowledge.

Available at: http://www.stroke.org
Age-Adjusted Death Rates for CHD, Stroke, Lung and Breast for White and Black Females (United States: 2006)

- **Coronary Heart Disease**
  - White Females: 101.5
  - Black Females: 130.0

- **Stroke**
  - White Females: 41.1
  - Black Females: 57.0

- **Lung Cancer**
  - White Females: 41.1
  - Black Females: 39.0

- **Breast Cancer**
  - White Females: 22.9
  - Black Females: 31.6

Source: NCHS.
Hispanics & Stroke

- Higher incidence among Mexican Americans than Caucasians

- Mexican Americans are at increased risk for all types of stroke and TIA at younger ages than Caucasians

- Spanish-speaking Hispanics are less likely to know stroke symptoms than English-speaking Hispanics, AA & Caucasians

Available at: http://www.stroke.org
Acute Stroke Treatments

• **Ischemic stroke (Brain Clot)**
  – Clot busting medication
    • t-PA (Tissue Plasminogen Activator)
• **Clot-removing devices**
  – Merci Retriever
  – Penumbra
• **Hemorrhagic Stroke (Brain Bleed)**
  – Clipping
  – Coiling

Available at: http://www.stroke.org
Race/Ethnicity, Quality of Care, and Outcomes in Ischemic Stroke

Lee H. Schwamm, MD; Mathew J. Reeves, PhD; Wenqin Pan, PhD; Eric E. Smith, MD, MPH; Michael R. Frankel, MD; DaiWai Olson, PhD, RN; Xin Zhao, MS; Eric Peterson, MD, MPH; Gregg C. Fonarow, MD
Race/Ethnicity, Quality of Care, and Outcomes in Ischemic Stroke

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Background—Prior studies suggest differences in stroke care associated with race/ethnicity. We sought to determine whether such differences existed in a population of black, Hispanic, and white patients hospitalized with stroke among hospitals participating in a quality-improvement program.

Methods and Results—We analyzed in-hospital mortality and 7 stroke performance measures among 397,257 patients admitted with ischemic stroke to 1181 hospitals participating in the Get With The Guidelines-Stroke program 2003 through 2008. Relative to white patients, black and Hispanic patients were younger and more often had diabetes mellitus and hypertension. After adjustment for both patient- and hospital-level variables, black patients had lower odds relative to white patients of receiving intravenous thrombolysis (odds ratio [OR], 0.84; 95% confidence interval [CI], 0.77 to 0.91), deep vein thrombosis prophylaxis (OR, 0.88; 95% CI, 0.83 to 0.92), smoking cessation (OR, 0.85; 95% CI, 0.79 to 0.91), discharge antithrombotics (OR, 0.88; 95% CI, 0.84 to 0.92), anticoagulants for atrial fibrillation (OR, 0.84; 95% CI, 0.75 to 0.94), and lipid therapy (OR, 0.91; 95% CI, 0.88 to 0.96), and of dying in-hospital (OR, 0.90; 95% CI, 0.85 to 0.95). Hispanic patients received similar care as their white counterparts on all 7 measures and had similar in-hospital mortality. Black (OR, 1.31; 95% CI, 1.28 to 1.35) and Hispanic (OR, 1.16; 95% CI, 1.11 to 1.20) patients had higher odds of exceeding the median length of hospital stay relative to whites. During the study, quality of care improved in all 3 race/ethnicity groups.

Conclusions—Black patients with stroke received fewer evidence-based care processes than Hispanic or white patients. These differences could lead to increased risk of recurrent stroke. Quality of care improved substantially in the Get With The Guidelines-Stroke Program over time for all 3 racial/ethnic groups. (Circulation. 2010;121:1492-1501.)
Race/Ethnicity, Quality of Care, & Outcomes in Ischemic Stroke

- 397,257 patients admitted w/ ischemic stroke to 1181 GWTG-Stroke hospitals
- April 1, 2003 - September 30, 2008

Patient Characteristics
- 52.7% women; age 71.1± 14.5 (SD) yrs
- 79.1% white, 16% black, and 4.9% Hispanic

- 7 evidence-based performance measurements to evaluate quality of care
- Hospital characteristics evaluated

Results

- Guideline based-care provided blacks vs. whites receiving:
  - IV thrombolysis (OR 0.84; 0.77-0.91),
  - DVT prophylaxis (OR 0.88; 0.83-0.92),
  - discharge anti-thrombotics (OR 0.88; 0.84-0.92),
  - anticoagulation for atrial fibrillation (OR 0.84; 0.75-0.94),
  - smoking cessation (OR 0.85; 0.79-0.91),
  - cholesterol lowering meds (OR 0.91; 0.88-0.96),
  - and quality of care (OR 0.90; 0.88-0.93)

Race/Ethnicity, Quality of Care, & Outcomes in Ischemic Stroke

Author’s Conclusion

– The GWTG-Stroke quality improvement program has the potential to accelerate the use of evidence-based and guideline-recommended therapies by improving provider knowledge and education on how to treat hospitalized stroke patients

Case

• A 57 year-old African American man with a Hx of HTN comes to your office concerned as his mother just died at 79 yo after an ischemic stroke.

• He wants to know what primary preventative interventions can reduce his chances of having a similar event.
HTN: Age-adjusted Prevalence

NHANES 2005-06

Age-adjusted Prevalence (%)

Consequences of Hypertension: Organ Damage

Hypertension

- TIAs, stroke, dementia
- Retinopathy
- Peripheral arterial disease
- LVH, CHD, CHF, AF
- Chronic kidney disease

AF=atrial fibrillation; CHD=coronary heart disease; HF=heart failure; LVH=left ventricular hypertrophy. Chobanian AV et al. *JAMA.* 2003;289:2560-2572.
Sites of Action of Major Antihypertensive Drug Classes

- **Diuretics**: Kidney tubules
- **β-Blockers**: Heart
- **Calcium channel Blockers**: Vascular smooth muscle
- **ACEI**: Angiotensin I to Angiotensin II
- **ARB**: AT₁ receptors

Renin-angiotensin system

The Renin-Angiotensin System

ACE = Angiotensin-converting enzyme; ARB = Angiotensin receptor blocker; CAGE = Chymase-angiotensin generating enzyme.

Adapted from Hollenberg 1998.
Concerns: BP Drugs in Blacks

• As monotherapy, diuretic or CCB usually more effective lowering BP, but nearly all patients need 2 drugs

• Cough & angioedema w/ ACEIs more likely in blacks than whites

ALLHAT: initial diuretic more effective ↓ BP & preventing stroke & combined CVD events in blacks than an ACEI

• AASK: ACEI more effective than CCB or β-blocker in limiting renal function decline

• LIFE: higher risk of CVD events w/ β-blocker vs. an ARB

Atrial Fibrillation

Normal electrical pathways

Abnormal electrical pathways

Sinus (SA) node

Atrioventricular (AV) node

Normal sinus rhythm

Atrial fibrillation
Left Atrial Thrombus in AF Patient

A  Left Atrium

B  Left Atrial Appendage Clot

## Anticoagulation

- **CHADS2:**
  - CHF: 1
  - Hypertension: 1
  - Age >75: 1
  - DM: 1
  - Stroke: 2

<table>
<thead>
<tr>
<th>Score</th>
<th>Annual Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1.9%</td>
</tr>
<tr>
<td>1</td>
<td>2.8%</td>
</tr>
<tr>
<td>2</td>
<td>4.0%</td>
</tr>
<tr>
<td>3</td>
<td>5.9%</td>
</tr>
<tr>
<td>4</td>
<td>8.5%</td>
</tr>
<tr>
<td>5</td>
<td>12.5%</td>
</tr>
<tr>
<td>6</td>
<td>18.2%</td>
</tr>
</tbody>
</table>

Score
- 0: Aspirin
- 1: Aspirin or warfarin
- 2 or more: Coumadin

AFRICAN AMERICANS HAVE SIGNIFICANTLY LOWER PREVALENCE OF AF DESPITE HIGHER PREVALENCE OF RISK FACTORS
Ethnic Distribution of ECG Predictors of Atrial Fibrillation and Its Impact on Understanding the Ethnic Distribution of Ischemic Stroke in the Atherosclerosis Risk in Communities (ARIC) Study

Soliman EZ et al. Stroke. 2009;40:1204-1211
Prevalence of Atrial Fibrillation Between African American and Caucasian Patients Hospitalized with Heart Failure

AF and African Americans (AA)

• Paradox of lower AF incidence & prevalence among AA despite higher common RFs
• Even with lower incidence and prevalence amongst AA, there might be disparity in diagnosis
• Black patients with AF less likely aware of diagnosis, and significantly less treated with appropriate anticoagulation (warfarin)
• Disproportionately higher incidence stroke amongst blacks complex and likely multifactorial w/ other contributors such as racial differences in genetic polymorphisms & ANS playing a role
AHA/ASA Guideline

Primary Prevention of Ischemic Stroke

A Guideline From the American Heart Association/American Stroke Association Stroke Council: Cosponsored by the Atherosclerotic Peripheral Vascular Disease Interdisciplinary Working Group; Cardiovascular Nursing Council; Clinical Cardiology Council; Nutrition, Physical Activity, and Metabolism Council; and the Quality of Care and Outcomes Research Interdisciplinary Working Group

The American Academy of Neurology affirms the value of this guideline.

Larry B. Goldstein, MD, FAAN, FAHA, Chair; Robert Adams, MS, MD, FAHA; Mark J. Alberts, MD, FAHA; Lawrence J. Appel, MD, MPH, FAHA; Lawrence M. Brass, MD, FAHA; Cheryl D. Bushnell, MD, MHS, FAHA; Antonio Culebras, MD, FAAN, FAHA; Thomas J. DeGraba, MD, FAHA; Philip B. Gorelick, MD, MPH, FAAN, FAHA; John R. Guyton, MD, FAHA; Robert G. Hart, MD, FAHA; George Howard, DrPH, FAHA; Margaret Kelly-Hayes, RN, EdD, MS, FAHA; J.V. (Ian) Nixon, MD, FAHA; Ralph L. Sacco, MD, MS, FAAN, FAHA

Vascular Disease: A Generalized and Progressive Process

Atherosclerosis → Thrombosis

Unstable angina
MI
Ischemic stroke/TIA
Critical leg ischemia
Cardiovascular death

Stable angina
Intermittent claudication

JUPITER Study Design

4 Week Placebo Run-in

No History of CVD

Men ≥50 years;

Women ≥60 years

LDL-C <130 mg/dL,

hsCRP levels ≥2.0 mg/L

Rosuvastatin 20 mg (n=8901)

Placebo (n=8901)

3-4 Years

Screening Visit

Randomization Visit

Safety Visit

Bi-Annual Visit

Final Visit

LDL-C

hsCRP

Lipids

hsCRP

LFTs

HbA1c


**JUPITER**

Individual Components of the Primary Endpoint

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Rosuvastatin</th>
<th>Placebo</th>
<th>HR</th>
<th>95%CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary Endpoint</strong>*</td>
<td>142</td>
<td>251</td>
<td>0.56</td>
<td>0.46-0.69</td>
<td>&lt;0.00001</td>
</tr>
<tr>
<td>Non-fatal MI</td>
<td>22</td>
<td>62</td>
<td>0.35</td>
<td>0.22-0.58</td>
<td>&lt;0.00001</td>
</tr>
<tr>
<td>Any MI</td>
<td>31</td>
<td>68</td>
<td>0.46</td>
<td>0.30-0.70</td>
<td>&lt;0.00002</td>
</tr>
<tr>
<td>Non-fatal Stroke</td>
<td>30</td>
<td>58</td>
<td>0.52</td>
<td>0.33-0.80</td>
<td>0.003</td>
</tr>
<tr>
<td>Any Stroke</td>
<td>33</td>
<td>64</td>
<td>0.52</td>
<td>0.34-0.79</td>
<td>0.002</td>
</tr>
<tr>
<td>Revascularization or Unstable Angina</td>
<td>76</td>
<td>143</td>
<td>0.53</td>
<td>0.40-0.70</td>
<td>&lt;0.00001</td>
</tr>
<tr>
<td>MI, Stroke, CV Death</td>
<td>83</td>
<td>157</td>
<td>0.53</td>
<td>0.40-0.69</td>
<td>&lt;0.00001</td>
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</table>

*Nonfatal MI, nonfatal stroke, revascularization, unstable angina, CV death

Primary Endpoint – Subgroup Analysis I

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>N</th>
<th>P for Interaction</th>
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</thead>
<tbody>
<tr>
<td>Men</td>
<td>11,001</td>
<td>0.80</td>
</tr>
<tr>
<td>Women</td>
<td>6,801</td>
<td></td>
</tr>
<tr>
<td>Age &lt; 65</td>
<td>8,541</td>
<td>0.32</td>
</tr>
<tr>
<td>Age &gt; 65</td>
<td>9,261</td>
<td></td>
</tr>
<tr>
<td>Smoker</td>
<td>2,820</td>
<td>0.63</td>
</tr>
<tr>
<td>Non-Smoker</td>
<td>14,975</td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>12,683</td>
<td>0.57</td>
</tr>
<tr>
<td>Non-Caucasian</td>
<td>5,117</td>
<td></td>
</tr>
<tr>
<td>USA/Canada</td>
<td>6,041</td>
<td>0.51</td>
</tr>
<tr>
<td>Rest of World</td>
<td>11,761</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>10,208</td>
<td>0.53</td>
</tr>
<tr>
<td>No Hypertension</td>
<td>7,586</td>
<td></td>
</tr>
<tr>
<td>All Participants</td>
<td>17,802</td>
<td></td>
</tr>
</tbody>
</table>

Effects of Intensive Blood-Pressure Control in Type 2 Diabetes Mellitus

The ACCORD Study Group*
Systolic Pressures (mean ± 95% CI)

Mean # Meds
Intensive: 3.2  3.4  3.5  3.4
Standard: 1.9  2.1  2.2  2.3

Average after 1st year: 133.5 Standard vs. 119.3 Intensive, Delta = 14.2

The ACCORD Study Group. Published at www.nejm.org March 14, 2010 (10.1056/NEJMoa1001282)
# Primary & Secondary Outcomes

<table>
<thead>
<tr>
<th>Event</th>
<th>Intensive Events (%/yr)</th>
<th>Standard Events (%/yr)</th>
<th>HR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary</td>
<td>208 (1.87)</td>
<td>237 (2.09)</td>
<td>0.88 (0.73-1.06)</td>
<td>0.20</td>
</tr>
<tr>
<td>Total Mortality</td>
<td>150 (1.28)</td>
<td>144 (1.19)</td>
<td>1.07 (0.85-1.35)</td>
<td>0.55</td>
</tr>
<tr>
<td>Cardiovascular Deaths</td>
<td>60 (0.52)</td>
<td>58 (0.49)</td>
<td>1.06 (0.74-1.52)</td>
<td>0.74</td>
</tr>
<tr>
<td>Nonfatal MI</td>
<td>126 (1.13)</td>
<td>146 (1.28)</td>
<td>0.87 (0.68-1.10)</td>
<td>0.25</td>
</tr>
<tr>
<td>Nonfatal Stroke</td>
<td>34 (0.30)</td>
<td>55 (0.47)</td>
<td>0.63 (0.41-0.96)</td>
<td>0.03</td>
</tr>
<tr>
<td>Total Stroke</td>
<td>36 (0.32)</td>
<td>62 (0.53)</td>
<td>0.59 (0.39-0.89)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Also examined Fatal/Nonfatal HF (HR=0.94, p=0.67), a composite of fatal coronary events, nonfatal MI and unstable angina (HR=0.94, p=0.50) and a composite of the primary outcome, revascularization and unstable angina (HR=0.95, p=0.40)

The ACCORD Study Group. Published at www.nejm.org March 14, 2010 (10.1056/NEJMoA1001282)
Stroke Results

• Intensive BP management reduced rate of two closely correlated secondary end points:
  – Total stroke \((p=0.01)\) and nonfatal stroke \((p=0.03)\)
• Assuming this finding real, NNT to lower SBP level to prevent 1 stroke over 5 years was 89
• Effects c/w meta-analyses summarizing impact of 10 mmHg reduction SBP on strokes from observational studies \((RR=0.64)\) and drug treatment trials \((RR=0.59)\)

The ACCORD Study Group. Published at www.nejm.org March 14, 2010 (10.1056/NEJMoa1001282)
Carotid Stenosis

- Some benefit for endarterectomy in asymptomatic stenosis
  - >60% or >80% cut-offs
  - Must have a very low peri-operative risk of stroke and death to realize benefit (3%)

- Data less convincing than symptomatic trials

- When to screen? Who to screen?
Cervical Artery Dissection

- **Vertebral & Carotid Arteries**
  - Common etiology of stroke in young

- **Pathophysiology**
  - Most idiopathic

- **Risk Factors**
  - Vomiting, Coughing, Chiropractic

- **Presentation**
  - Neck Pain, HA

- **Treatment**
  - Anticoagulation
Platelet Cascade in Thrombus Formation

1. Adhesion
   - Platelets
   - Collagen
   - GP Ia/Ila bind
   - von Willebrand Factor/GP Ib bind
   - Lipid core

2. Activation
   - Thrombin
   - ADP
   - 5 HT
   - TXA₂

3. Aggregation
   - Activated GP IIb/IIIa
   - Fibrinogen
Mechanisms of Action of Oral Antiplatelet Therapies

ADP = adenosine diphosphate, TXA₂ = thromboxane A₂, COX = cyclooxygenase.
Antiplatelet Options

- 1. ASA
  - 50mg to 1.5g equal efficacy long-term
- 2.
  - 25mg ASA/200mg ER Dipyridamole (Aggrenox)
  - ESPS-2, ESPRIT (Lancet 5/06)
- 3. Clopidogrel (Plavix)
  - MATCH (Lancet 7/04)
  - FASTER (Lancet Neurol 10/07)
- 4. Prasugrel (Effient) (Wiviott SD NEJM 2007)
Clopidogrel response variability: Change the agent?

Prasugrel
Prodrug

Oxidation
(Cytochrome P450)

Hydrolysis
(Esterases)

Clopidogrel

85% Inactive metabolites
Esterases

Public Health Advisory:

Updated Safety Information about a drug interaction between

Clopidogrel Bisulfate (marketed as Plavix) & Omeprazole (marketed as Prilosec and Prilosec OTC)
FDA NEWS RELEASE
March 12, 2010

• FDA Announces New Boxed Warning on clopidogrel

• Alerts patients, health care professionals to potential for reduced effectiveness
New Clopidogrel Warning

"The frequency is about 2% of Caucasians, 4% of blacks, and 14% of Chinese."

Mary Ross Southworth, PharmD,
FDA Deputy Director for Safety
Division of Cardiovascular and Renal Products
“We will only be truly free when we reach down to the inner depths of our own being and sign with the pen and ink of assertive selfhood, our own emancipation proclamation. No civil rights, no voting rights, no equal rights, no immigration rights are worth fighting for if we are dying from heart disease and stroke.”

Yolanda King
(Daughter of Dr. Martin Luther King & Coretta Scott King – Died in 2006 of a stroke)