Geographic Variations in Stroke Incidence and Mortality Among Older Populations in Four US Communities

Aiman El-Saed, MD, PhD, MPH; Lewis H. Kuller, MD, DrPH; Anne B. Newman, MD, MPH; Oscar Lopez, MD; Joseph Costantino, DrPH; Kathleen McTigue, MD, MS, MPH; Mary Cushman, MD, MSc; Richard Kronmal, PhD

Background and Purpose—Stroke is a leading cause of death and disability in the US. There is limited data on geographic variations in stroke incidence among older US populations who experience the majority of stroke burden. The purpose of this study was to compare stroke incidence and mortality rates in 4 US communities.

Methods—Participants in the Cardiovascular Health Study (CHS) who had no history of stroke at baseline (n=5639) were followed for 10 or 7 years in predominantly white (n=5002) and black (n=637) participants, respectively. Incident stroke was validated by a stroke adjudication committee after ascertainment at annual visits, interim telephone contacts, and review of Medicare hospitalization data.

Results—The 2000 US population age and sex standardized total stroke incidence rate for all CHS participants was 17.7 per 1000 person-years (95% CI: 15.9, 19.5). The rate was significantly lower in Allegheny County, Pennsylvania 9.6/1000 person-years (95% CI: 7.7, 11.5) than Forsyth County, North Carolina 19.2/1000 person-years (95% CI: 15.6, 22.8), Sacramento County, California 20.7/1000 person-years (95% CI: 16.9, 24.5), and Washington County, Maryland 19.8/1000 person-years (95% CI: 16.1, 23.5). The lower stroke incidence rate in Allegheny County was consistent in gender, race, and age groups. Though not statistically significant, stroke mortality was also lower in Allegheny County than other 3 sites. The 1-month case fatality rate was similar in the 4 sites for all strokes, and by stroke types.

Conclusions—Understanding geographic variations in stroke incidence may be an important step in improving preventive practices of stroke. (Stroke. 2006;37:1975-1979.)

Key Words: epidemiology ■ incidence ■ geography ■ mortality ■ stroke
TABLE 1. CHS Participant Characteristics at Baseline by Site

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Forsyth County, NC n (%)</th>
<th>Sacramento County, CA n (%)</th>
<th>Washington County, MD n (%)</th>
<th>Allegheny County, PA n (%)</th>
<th>Total n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total No. of those at risk for stroke at baseline</td>
<td>1488 (100.0%)</td>
<td>1471 (100.0%)</td>
<td>1251 (100.0%)</td>
<td>1429 (100.0%)</td>
<td>5639 (100.0%)</td>
</tr>
<tr>
<td>Cohort</td>
<td>Original cohort</td>
<td>New cohort</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1266 (85.1%)</td>
<td>222 (14.9%)</td>
<td>204 (13.9%)</td>
<td>NA</td>
<td>211 (14.8%)</td>
<td>5002 (88.7%)</td>
</tr>
<tr>
<td>Baseline Age</td>
<td>65–74 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>997 (67.0%)</td>
<td>801 (64.0%)</td>
<td>NA</td>
<td>972 (68.0%)</td>
<td>3759 (66.7%)</td>
<td></td>
</tr>
<tr>
<td>75–84 years</td>
<td>443 (29.8%)</td>
<td>394 (31.5%)</td>
<td>411 (28.8%)</td>
<td>1668 (29.6%)</td>
<td></td>
</tr>
<tr>
<td>85+ years</td>
<td>48 (3.2%)</td>
<td>56 (4.5%)</td>
<td>46 (3.2%)</td>
<td>212 (3.8%)</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td>Males</td>
<td>Females</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>900 (60.5%)</td>
<td>850 (57.8%)</td>
<td>726 (58.0%)</td>
<td>811 (56.8%)</td>
<td>3287 (58.3%)</td>
<td></td>
</tr>
<tr>
<td>588 (39.5%)</td>
<td>621 (42.2%)</td>
<td>525 (42.0%)</td>
<td>618 (43.2%)</td>
<td>2352 (41.7%)</td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td>Whites</td>
<td>Blacks</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1154 (78.0%)</td>
<td>1228 (84.6%)</td>
<td>1238 (99.1%)</td>
<td>1123 (79.0%)</td>
<td>4743 (84.7%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>326 (22.0%)</td>
<td>224 (15.4%)</td>
<td>11 (0.9%)</td>
<td>299 (21.0%)</td>
<td>860 (15.3%)</td>
</tr>
</tbody>
</table>

NA indicates not applicable.

Outcome Assessment
Ascertainment methods of incident and prevalent stroke in CHS have been described. Excessive historical, physical and laboratory evaluations were performed at baseline for each cohort to identify prevalent strokes, and these were validated by a committee. 12 ICD-9-CM codes 430 to 438 were investigated for possible stroke events. Ascertainment of new stroke events was carried out by interview at annual visits and interim telephone contacts, from notification of events by participants, and reviewing Medicare hospitalization data. For suspected stroke events, clinical records were sought, and copies including admission and discharge notes, results of pertinent tests, and copies of any brain images (CT and MRI) were obtained. 13 Provisional diagnoses of stroke were reviewed and adjudicated at periodic meetings of a cerebrovascular disease end-point committee. The committee also classified the stroke subtype and determined whether death was caused by stroke. 14 Information for classification of death was obtained from death certificates, autopsy and coroner’s reports (if available), hospital records, and interviews with attending physicians, next-of-kin, and witnesses. 12

Statistical Analysis
Participants with prebaseline stroke were excluded from all analyses. Incident stroke cases were adjudicated from the baseline examination for each cohort through June 30, 2000. Years of follow-up were defined as the time from the baseline visit to occurrence of stroke for those who had a stroke and as the time from the baseline visit to censoring (death or drop out) for those who did not have a stroke. Stroke incidence rates per 1000 person-years were calculated by dividing the number of new stroke events by the person-years at risk. Stroke mortality rate was calculated as the number of adjudicated stroke deaths within a month after stroke divided by the person-years at risk. Incidence rates were compared across the sites for all participants and by race, gender, and baseline age groups (65 to 74, 75 to 84, and 85 years and older). Stroke rates were either age-specific or age-standardized. Rates were also sex-standardized when applicable. Age standardization was done using the 2000 US census population distribution using the direct method. Stroke case fatality rates were calculated by dividing the number of fatal strokes by all new strokes. Fatal and nonfatal cumulative stroke hazards over the total follow-up period were calculated using a Cox regression with adjustment for age, race and gender. The models were then stratified by site.

Results
Demographics
The total number of participants at risk for incident stroke at baseline in the 4 sites was 5639. Of these, 5002 (88.7%) were recruited between 1989 and 1990 (original cohort) and 637 (11.3%) recruited between 1992 and 1993 (new cohort). The mean age at baseline was 72.8 years (median 72 years, range 65 to 100 years); 3759 (66.7%) participants were aged 65 to 74 years, 1668 (29.6%) were 75 to 84 years, and 212 (3.8%) were 85 or more years old. 58% of the participants were women. There were no significant age or gender differences between sites. Approximately 85% of the participants were white and 15% were black with a lower percentage of blacks at the Washington County site (Table 1).

Stroke Incidence Rates
Over an average of 8.6 years of follow-up (median 10.2) in the original cohort and 6.3 years (median 7.2) in the new cohort (total 46 976 person-years), there were 665 incident strokes in the 4 sites combined. The 2000 US population age- and sex-standardized total stroke incidence rate for all CHS communities: Forsyth County, NC; Sacramento County, CA; Washington County, MD; and Allegheny County, PA. Potentially eligible participants were excluded if they were institutionalized, wheelchair-bound in the home, or were receiving cancer treatment. The Allegheny County site population was entirely urban, and the other 3 centers recruited a mixture of urban and rural populations. 5888 men and women were recruited in 2 waves. A total of 5201 participants were recruited in 1989 to 1990 in the first wave (original cohort). Because blacks were under-represented in the first wave of the study, additional 687 black participants were recruited in 1992 to 1993 in a second wave (new cohort), to improve the racial representativeness of the study. Differences between those recruited and those not recruited have been presented elsewhere. 13
participants was 17.7 per 1000 person-years (95% CI: 15.9, 19.5). The rates were significantly lower in Allegheny County (9.6; 95% CI: 7.7, 11.5) than Forsyth County (19.2; 95% CI: 15.6, 22.8), Sacramento County (20.7; 95% CI: 16.9, 24.5), and Washington County (19.8; 95% CI: 16.1, 23.5). Age-standardized rates were significantly lower in Allegheny County for women and whites. The rates were also lower, but not statistically significant, in Allegheny County for men and blacks (Table 2). Age-specific stroke incidence rate steadily increased with increasing age groups at all 4 sites. Allegheny County had a lower total stroke incidence rate than the other 3 sites among all age groups; statistical significance of this difference varied by age groups (Figure). The distribution of incidence of different stroke types was similar among the 4 sites (P=0.68): overall 85% of strokes were ischemic, 10% hemorrhagic and 5% undefined stroke type.

### TABLE 2. Age Standardized Total Stroke Incidence Rates per 1000 Person-Years of CHS Participants by Gender, Race and Site

<table>
<thead>
<tr>
<th></th>
<th>Forsyth County, NC</th>
<th>Sacramento County, CA</th>
<th>Washington County, MD</th>
<th>Allegheny County, PA</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Events</td>
<td>Events</td>
<td>Events</td>
<td>Events</td>
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<tr>
<td>P-Y</td>
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<td>P-Y</td>
<td>P-Y</td>
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<td>P-Y</td>
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<tr>
<td>Rate</td>
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<td>Rate</td>
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<tr>
<td>95% CI</td>
<td>95% CI</td>
<td>95% CI</td>
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<td>95% CI</td>
<td>95% CI</td>
</tr>
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</table>

#### Gender:

<table>
<thead>
<tr>
<th></th>
<th>Males</th>
<th>Females</th>
<th></th>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>71</td>
<td>114</td>
<td>79</td>
<td>121</td>
<td>15.6, 24.0</td>
<td>12.1, 19.9</td>
</tr>
<tr>
<td>Rate</td>
<td>4583.5</td>
<td>4998.9</td>
<td>4015.4</td>
<td>41</td>
<td>15.4, 26.8</td>
<td>15.4, 26.8</td>
</tr>
<tr>
<td>95% CI</td>
<td>17.8</td>
<td>16.0</td>
<td>21.1</td>
<td>60</td>
<td>8.3, 16.1</td>
<td>8.3, 16.1</td>
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</table>

#### Race:

<table>
<thead>
<tr>
<th></th>
<th>Whites</th>
<th>Blacks</th>
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<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>143</td>
<td>41</td>
<td>172</td>
<td>27</td>
<td>15.2, 24.2</td>
<td>21.4, 22.5</td>
</tr>
<tr>
<td>Rate</td>
<td>9930.8</td>
<td>2333.3</td>
<td>10 677.5</td>
<td>1491.4</td>
<td>18.4, 22.9</td>
<td>18.8, 22.8</td>
</tr>
<tr>
<td>95% CI</td>
<td>18.4</td>
<td>21.4</td>
<td>19.8</td>
<td>20.2</td>
<td>14.3, 22.5</td>
<td>14.3, 22.5</td>
</tr>
</tbody>
</table>

#### Total:

|       | 185    | 114    | 200  | 12 221.9 | 15.5, 22.7 | 16.2, 22.8 |
| Rate  | 9905.9 | 10 292.1 | 2084.3 | 10 389.7 | 16.0, 23.3 | 16.0, 23.3 |
| 95% CI| 17.3   | 10.7   | 18.2 | 5.6, 10.6 | 8.2, 13.3 | 8.2, 13.3 |

P-Y indicates person-years.

*Age- and sex-standardized.

**Age-specific stroke incidence rates per 1000 person-years of CHS participants by site.**
Case Fatality and Mortality
For all CHS participants, the 1-month case fatality was 12.6% for all strokes, 8.1% for ischemic strokes, and 44.6% for hemorrhagic strokes. The 1-month case fatality percentages were similar in the 4 sites for all strokes ($P=0.95$) and by stroke types ($P=0.87$ for ischemic and $P=0.23$ for hemorrhagic). Though not statistically significant, age- and sex-standardized total stroke mortality rates per 1000 person-years were lower in Allegheny County (1.55; 95% CI: 0.77, 2.43) than Forsyth County (2.79; 95% CI: 1.34, 4.26), Sacramento County (2.67; 95% CI: 1.16, 4.24), and Washington County (3.07; 95% CI: 1.37, 4.83).

Cumulative Incidence and Mortality
The 10-year cumulative hazard for total incident stroke events adjusted for age, gender, and race was significantly lower ($P<0.001$) in Allegheny County (156 per 1000; 95% CI: 144.2, 167.8) compared with Forsyth County (172; 95% CI: 148.5, 195.5), Sacramento County (175; 95% CI: 153.4, 196.6), and Washington County (176; 95% CI: 150.5, 201.5). The 10-year cumulative hazard for fatal stroke events was lower, but not statistically significant, in Allegheny County compared with the other 3 sites after adjusting for age, gender and race ($P=0.47$). For all CHS participants, the cumulative hazard for fatal stroke events was 19 deaths per 1000 (95% CI: 15.1, 22.9).

Discussion
Overall Total Stroke Incidence
The unadjusted overall stroke incidence rate in this study is substantially higher than those reported in other similar stroke incidence studies in the US$^{14-16}$ because of the older age group in the CHS.$^{17}$ In previous reports the overall estimated annual stroke incidence rates among US whites ranged between 0.8 to 1.18 per 1000 in New York$^5$ to 1.61 to 3.16 in South Carolina$^4$ compared with 17.3 per 1000 person-years in the current report. The age-specific rates from this report, however, were not dramatically different than those reported in other studies. For example, the overall stroke incidence for those 75 to 84 years in the CHS was 21.9 per 1000 person-years compared with 12.2 (white) and 18.3 (black) per 1000 in Greater Cincinnati study$^8$ and 18.2 (white men) and 11.9 (white women) per 1000 in Rochester, Minnesota study.$^7$ In addition, using different overlapping ascertainment techniques in CHS$^{14,15}$ may have yielded higher ascertainment of stroke cases than other studies.$^4-10$

Age-specific rates in CHS were also comparable to those reported in other western countries. For example, comparing the CHS stroke incidence rates in those aged 85 years or older (32.7 per 1000 person-years) to other countries, as reviewed by Feigin et al.,$^{16}$ the CHS incidence was similar to Greece, Italy and Norway (26.6 to 30.4 per 1000), higher than France, the United Kingdom and Germany (18.2 to 21.2 per 1000), and lower than Japan (38.5 per 1000 in females and 49.2 per 1000 in males).

We did not observe significant differences in stroke incidence based on race or gender. This may reflect sample age, with older populations having less race and gender differences in stroke incidence. In previous reports, older age groups have a smaller black/white difference$^5,8,19$ and male/female difference$^5-7,20$ in stroke incidence compared with younger age groups. For example, the black/white risk ratio in the Greater Cincinnati study$^8$ decreased from 2.2 in those <35 years to 1.3 in those ≥85 years. The male/female risk in the Northern Manhattan Stroke Study$^5$ decreased steadily from 2.5-fold in those aged 45 to 54 years, reversing in those aged 85 years or older, when females had slightly higher stroke incidence than males.

Site-Specific Total Stroke Incidence
Despite similar total mortality and CHD morbidity (data not shown), we report significantly lower stroke incidence rates in Allegheny County than the other 3 CHS sites. The lower stroke incidence rate in Allegheny County was consistent over time and began as early as the fourth year of follow-up. It is possible that site differences in stroke incidence become clearer with increasing overall stroke rates later in follow-up. Site differences in stroke incidence may not be attributed to differential loss of follow-up between Allegheny and non-Allegheny sites because there was virtually no loss to follow-up in the CHS irrespective of site and even among those who did not attend a certain clinic visit, information was still obtained for clinical events mainly by phone contact, home or nursery home visit, or reviewing HCFA records. Moreover, both groups had similar mean stroke follow-up years; in addition, our stroke rates were calculated per 1000 person-years and not 1000 persons. Lower stroke incidence rates in Allegheny County were consistent with national vital statistics (1991–1998) showing lower age-adjusted stroke mortality rates per 1000 Americans age 35 years or older in Allegheny (1.10) compared with Forsyth (1.58), Sacramento (1.36), and Washington (1.18) Counties.$^{21}$ These differences in stroke mortality could be a function of the lower incidence rates or to differential case fatality. In another related manuscript$^{22}$ and after comparing many traditional and subclinical stroke risk factors, site differences in stroke risk factors at baseline and subsequent control through the follow-up period explained only about 30% of site differences in stroke incidence.

Forsyth County, NC was the only CHS site located in the “stroke belt” and according to national data,$^{23}$ ranked the highest for stroke mortality among the 4 studied counties. However, the stroke incidence rate in Forsyth County was similar to that in Sacramento County, CA and Washington County, MD. Although the population studied in Forsyth County is not representative of the whole stroke belt, this data may support the hypothesis that the “stroke belt” is not a static phenomenon, and could be related to temporal trends in a variety of medical, socioeconomic, and behavioral factors rather than the physical properties of southeastern US.$^{21}$

Stroke Mortality and Case Fatality
The 1-month case fatality rate of stroke in CHS was comparable to other US studies (10% to 15%).$^{4,5}$ The stroke mortality rate per 1000 person-years was also lower in Allegheny County (1.55) than the other 3 sites (2.79, 2.67, 3.07), although these differences were not statistically significant, probably because of limited power (84 fatal events). The lower mortality rate in Allegheny County than the other 3 sites might be explained by the lower incidence and similar case fatality and proportional frequencies of incident stroke
types in Allegheny County compared with the other 3 sites. In addition, total mortality (unlike stroke mortality) was similar between sites suggesting similar health care use.

Study Strengths and Limitations
This study has many strengths, including a prospective population-based design, central adjudication of events from 4 geographically separated sites, large sample size, and long-term follow-up. Nevertheless, the number of events was small for fatal strokes and for incident strokes in some groups as blacks and the very old (85 years and more). In addition, because CHS sites were chosen based on methodological applicability rather than geographic characteristics, it is difficult to generalize conclusions from the 4 CHS sites to different parts of US.

Conclusions
Stroke incidence rates increased with age at all 4 CHS sites, with little or no race or gender differences in incidence. Total stroke incidence rates were significantly lower in Allegheny County than other 3 sites. Though not statistically significant, the total stroke mortality rates were also lower in Allegheny County than other 3 sites. Understanding variations in stroke incidence may be an important step in improving preventive practices. Further investigation in ongoing studies is needed to clarify the undetermined causes of stroke incidence variation.

Disclosures
None.

References
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