A Multinational Comparison of Subarachnoid Hemorrhage Epidemiology in the WHO MONICA Stroke Study

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Background and Purpose—By official, mostly unvalidated statistics, mortality from subarachnoid hemorrhage (SAH) show large variations between countries. Using uniform criteria for case ascertainment and diagnosis, a multinational comparison of attack rates and case fatality rates of SAH has been performed within the framework of the WHO MONICA Project.

Methods—In 25- to 64-year-old men and women, a total of 3368 SAH events were recorded during 35.9 million person-years of observation in 11 populations in Europe and China. Strict MONICA criteria were used for case ascertainment and diagnosis of stroke subtype. Case fatality was based on follow-up at 28 days after onset.

Results—Age-adjusted average annual SAH attack rates varied 10-fold among the 11 populations studied, from 2.0 (95% CI 1.6 to 2.4) per 100 000 population per year in China-Beijing to 22.5 (95% CI 20.9 to 24.1) per 100 000 population per year in Finland. No consistent pattern was observed in the sex ratio of attack rates in the different populations. The overall 28-day case fatality rate was 42%, with 2-fold differences in age-adjusted rates between populations but little difference between men and women. Case fatality rates were consistently higher in Eastern than in Western Europe.

Conclusions—Using a uniform methodology, the WHO MONICA Project has shown very large variations in attack rates of SAH across 11 populations in Europe and China. The generally accepted view that women have a higher risk of SAH than men does not apply to all populations. Marked differences in outcome of SAH add to the wide gap in the burden of stroke between East and West Europe. (Stroke. 2000;31:1054-1061.)

Key Words: epidemiology ■ incidence ■ mortality ■ subarachnoid hemorrhage ■ World Health Organization

Studies of the epidemiology of subarachnoid hemorrhage (SAH) have shown remarkably divergent results. First, in population-based studies, crude incidence rates have been reported to range from 5.2 per 100 000 population per year in Valle d’Aosta, Italy, to 19.4 per 100 000 population per year in Middle Finland. 1 Second, although textbook knowledge states that SAH is more common in women than in men, there are reports that this may not be so in all populations. 2 Third, a commonly held view is that SAH is more common in younger age groups, but the epidemiological data supporting this contention are not consistent. 3 Fourth, wide variations in case fatality rates have been reported, ranging from <10% to >60%. 4

The discrepant epidemiological data on SAH may reflect true variations between populations, but may also be due to methodological differences between studies. Because immediate or very early death is common in SAH, 1 case ascertainment could be inaccurate in studies that do not evaluate coroner and death certificate data. Differences in study design (prospective, retrospective, or cross-sectional) may contribute to differences in results. The age range covered and the definitions of case fatality differ between studies, and methods for age adjustment of event and case fatality rates have not been consistent. The small number of SAH events in some of the studies makes the estimates uncertain because of poor statistical power. Whether there are variations in case ascertainment, diagnostic procedures, and other aspects of data quality is often difficult to assess.

The WHO MONICA Project (MONICA=Multinational Monitoring of Trends and Determinants in Cardiovascular Disease) was designed to overcome many of the difficulties involved in comparisons of cardiovascular epidemiology between populations and over time. 5 The MONICA studies were prospective and strictly population based. In the stroke component of the project, uniform methods for case ascertainment, interpretation of clinical presentation, and diagnostic procedures were used. 6 Extensive quality assessments were performed to ensure that the data were accurate. 7

Thus, the MONICA Project provided a unique possibility to compare stroke epidemiology between populations. In the
present study, the MONICA stroke database was used to describe the epidemiology of SAH in 11 populations: 5 in Western Europe, 5 in former socialist economies in Eastern Europe, and 1 in China.

Subjects and Methods

Study Populations

The main aim of the WHO MONICA Project was to analyze to what extent secular trends in myocardial infarction and stroke incidence rates were explained by changes in the prevalence of cardiovascular risk factors, such as hypercholesterolemia, hypertension, and cigarette smoking in the populations studied. In the years 1982 to 1986, 14 of the MONICA Collaborating Centers (MCCs) entered the stroke component of the project. In the present cross-sectional comparison of the epidemiology of SAH, data from 11 of the MCCs in 10 countries was included. The reasons for exclusion of 3 MCCs were uncertainties about data quality (1 Russian and 1 Hungarian center) and early termination of collection of stroke data (1 German center) and “insufficient data” by the MONICA criteria. To ensure that ad-

Case Ascertainment and Evaluation

Case ascertainment was population based, ie, it included both hospitalized and nonhospitalized cases (for SAH, mainly those who died before receiving medical attention). For each event identified by the local stroke register, a core data record form was submitted to the MONICA Data Center in Helsinki, Finland. Suspected stroke events that were registered include all cases with a clinical diagnosis of acute stroke (International Classification of Diseases, Ninth Revision [ICD-9] codes 430 to 434 and 436) after treatment in hospital or on an outpatient basis, and all fatal cases in the study population with ICD-9 codes 430 to 436 given on the death certificate. Each MCC also performed a preliminary screening of cases with selected nonstroke diagnoses to identify commonly occurring types of misclassification and include such diagnoses in those regularly screened. All cases of sudden death in the populations were initially reviewed for possible inclusions in the coronary artery disease MONICA registers. If the criteria for a coronary death were not fulfilled, the case was validated as a possible death from stroke (including SAH).

On the basis of all the available information, the local MONICA team then classified the event as “definite stroke,” “definite stroke associated with definite myocardial infarction,” “not stroke,” or “insufficient data” by the MONICA criteria. To ensure that ad-

Table 1. WHO MONICA Populations: 1989 Population Size, Years Included in Study, Person-Years of Observation, and Number of SAH Events for the Population Aged 25–64 Years

<table>
<thead>
<tr>
<th>MONICA Center</th>
<th>Population in 1989</th>
<th>Period of Observation</th>
<th>Years of Observation</th>
<th>Person-Years</th>
<th>Total No. of SAH Events</th>
<th>Fatal SAH Events*</th>
</tr>
</thead>
<tbody>
<tr>
<td>China-Beijing</td>
<td>463 492</td>
<td>1984–1993</td>
<td>10</td>
<td>4 634 920</td>
<td>85</td>
<td>19</td>
</tr>
<tr>
<td>Denmark-Glostrup</td>
<td>181 190</td>
<td>1982–1991</td>
<td>10</td>
<td>1 811 900</td>
<td>198</td>
<td>81</td>
</tr>
<tr>
<td>East Germany</td>
<td>747 075</td>
<td>1984–1989</td>
<td>6</td>
<td>4 482 450</td>
<td>225</td>
<td>94</td>
</tr>
<tr>
<td>Italy-Friuli</td>
<td>509 390</td>
<td>1984–1993</td>
<td>10</td>
<td>5 093 900</td>
<td>423</td>
<td>165</td>
</tr>
<tr>
<td>Lithuania-Kaunas</td>
<td>219 009</td>
<td>1986–1995</td>
<td>10</td>
<td>2 190 090</td>
<td>215</td>
<td>110</td>
</tr>
<tr>
<td>Poland-Warsaw</td>
<td>277 651</td>
<td>1984–1994</td>
<td>11</td>
<td>3 054 161</td>
<td>306</td>
<td>126</td>
</tr>
<tr>
<td>Russia-Moscow</td>
<td>462 850</td>
<td>1985–1993</td>
<td>9</td>
<td>4 165 650</td>
<td>276</td>
<td>166</td>
</tr>
<tr>
<td>Sweden-Göteborg</td>
<td>224 657</td>
<td>1984–1994</td>
<td>11</td>
<td>2 471 227</td>
<td>244</td>
<td>80</td>
</tr>
<tr>
<td>Yugoslavia-Novisad</td>
<td>153 926</td>
<td>1983–1995</td>
<td>13</td>
<td>2 001 038</td>
<td>128</td>
<td>81</td>
</tr>
</tbody>
</table>

*Number of persons who had a subarachnoid hemorrhage and died within 28 days of the onset of symptoms.

Table 2. WHO MONICA Populations: Average Annual Subarachnoid Hemorrhage Attack Rates per 100 000 Population for Men and Women Aged 25–64 Years

<table>
<thead>
<tr>
<th>MONICA Center</th>
<th>Men (95% CI)</th>
<th>Women (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>China-Beijing</td>
<td>1.9 (1.3–2.5)</td>
<td>2.0 (1.4–2.6)</td>
</tr>
<tr>
<td>East Germany</td>
<td>5.0 (4.1–5.9)</td>
<td>4.8 (3.9–5.7)</td>
</tr>
<tr>
<td>Yugoslavia-Novisad</td>
<td>6.5 (3.9–8.1)</td>
<td>5.7 (4.2–7.2)</td>
</tr>
<tr>
<td>Russia-Moscow</td>
<td>8.6 (7.3–9.9)</td>
<td>4.8 (3.9–5.7)</td>
</tr>
<tr>
<td>Italy-Friuli</td>
<td>7.4 (6.3–8.5)</td>
<td>7.8 (6.7–8.9)</td>
</tr>
<tr>
<td>Lithuania-Kaunas</td>
<td>10.2 (8.2–12.2)</td>
<td>9.3 (7.6–11.0)</td>
</tr>
<tr>
<td>Poland-Warsaw</td>
<td>10.9 (9.2–12.6)</td>
<td>9.1 (7.6–10.6)</td>
</tr>
<tr>
<td>Sweden-Göteborg</td>
<td>9.1 (7.4–10.8)</td>
<td>11.0 (9.1–12.9)</td>
</tr>
<tr>
<td>Denmark-Glostrup</td>
<td>8.8 (6.9–10.7)</td>
<td>12.3 (10.0–14.6)</td>
</tr>
<tr>
<td>Northern Sweden</td>
<td>15.2 (13.1–17.3)</td>
<td>20.6 (18.1–23.1)</td>
</tr>
<tr>
<td>Finland</td>
<td>26.0 (23.6–28.4)</td>
<td>18.7 (16.6–20.8)</td>
</tr>
</tbody>
</table>

Figure 1. Age-adjusted average annual SAH attack rates per 100 000 population (age-adjusted to Segi’s world population). Horizontal lines indicate 95% CIs.
Classification of Stroke Subtypes

Cases identified as “definite stroke” were classified into stroke subtypes. For a diagnosis of SAH, at least 1 of the following criteria had to be met: (1) recent SAH and an aneurysm or arteriovenous malformation at autopsy, (2) a CT finding of blood in the sylvian fissure or between the frontal lobes or in the basal cistern or in the cerebral ventricles, (3) bloody cerebrospinal fluid (>2,000 erythrocytes/mm³) and an aneurysm or an arteriovenous malformation found on angiography, or (4) bloody (>2,000 erythrocytes/mm³) and xanthochromatic cerebrospinal fluid and the possibility of intracerebral hemorrhage excluded by necropsy or CT examination. Thus, in every case included in the study, the diagnosis had been confirmed by CT scan, CSF examination, or at autopsy.

The study protocol (MONICA Manual) emphasized the need for uniform diagnostic criteria and data collection between MCCs and throughout the study period. All data submitted to the MONICA Data Center were checked for consistency and completeness. To ensure uniformity in coding, sets of test cases were distributed to all MONICA stroke centers and feedback was provided. The test case histories included relevant clinical information on actual patients, and they were collected from all participating MCCs. Data submitted to the MONICA Data Center was subjected to logic and consistency checks. Results of detailed quality assessments of case ascertainment and diagnostic procedures in the stroke component of the MONICA Project have been published.

Definitions of Event Rates and Statistical Analyses

In accordance with the MONICA definitions, “attack rates” referred to the number of all SAH events (both first and recurrent) per 100,000 person-years of observation. “Fatal events” in the MONICA stroke study were defined as death within the first 28 days after onset; “case fatality” was the proportion of fatal events out of all events. Congruent with the registration of acute myocardial infarction events in the MONICA study, only definite stroke events with an SAH diagnosis were included in nonfatal cases, but both the definite stroke and unclassifiable data categories were included in fatal cases.

The attack rate determinations, the denominator (number of person-years of observation) for each MCC was calculated by multiplying the population in 1989 by the number of years of observation. Attack rates were standardized using Segi’s world population weights for the 5-year age groups 25–29, 30–34, 35–39, 40–44, 45–49, 50–54, 55–59, and 60–64 years old). The 95% CIs were calculated with the normal approximation of binomial distribution. The statistical package SPSS 8.0 (SPSS, Inc) was used to perform all statistical analyses.

Results

The total number of SAH events in the 11 populations was 3,368, of which 1,404 (41.7%) were fatal within 28 days of onset (Table 1). The population in 1989, the period of observation, and the number of person-years of observation used to calculate the event rates for each MCC are shown in Table 1. For the population of the 11 MCCs combined, there was little difference between men and women in the average age at the time of onset of the SAH. The average (±SD) age was 49.0±10.0 years for the total population, 49.8±10.0 years for men, and 48.1±10.0 years for women. The average age of onset for the total population was similar among the individual MCCs and ranged from 48.6 years in Poland to 51.4 years in China (all within the 25–64 year age range).

TABLE 3. WHO MONICA Populations: Age-Specific Average Annual SAH Attack Rates per 100,000 Population for the Population Aged 25–64 Years

<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>China-Beijing</td>
<td>0.6</td>
<td>0.2</td>
<td>0.3</td>
<td>1.3</td>
<td>2.7</td>
<td>3.7</td>
<td>4.2</td>
<td>5.2</td>
</tr>
<tr>
<td>East Germany</td>
<td>3.1</td>
<td>2.9</td>
<td>4.9</td>
<td>4.5</td>
<td>5.2</td>
<td>6.9</td>
<td>8.5</td>
<td>5.3</td>
</tr>
<tr>
<td>Russia-Moscow</td>
<td>1.3</td>
<td>2.1</td>
<td>3.7</td>
<td>7.5</td>
<td>10.7</td>
<td>9.1</td>
<td>9.6</td>
<td>13.5</td>
</tr>
<tr>
<td>Yugoslavia-Novis Sad</td>
<td>0.8</td>
<td>1.8</td>
<td>2.6</td>
<td>4.1</td>
<td>11.5</td>
<td>10.3</td>
<td>10.0</td>
<td>14.2</td>
</tr>
<tr>
<td>Italy-Friuli</td>
<td>1.7</td>
<td>2.7</td>
<td>5.6</td>
<td>6.5</td>
<td>9.6</td>
<td>12.4</td>
<td>16.0</td>
<td>14.5</td>
</tr>
<tr>
<td>Sweden-Goteborg</td>
<td>1.7</td>
<td>4.3</td>
<td>4.8</td>
<td>10.7</td>
<td>14.9</td>
<td>17.1</td>
<td>19.1</td>
<td>17.1</td>
</tr>
<tr>
<td>Lithuania-Kaunas</td>
<td>3.5</td>
<td>5.1</td>
<td>5.1</td>
<td>8.0</td>
<td>11.5</td>
<td>19.2</td>
<td>17.5</td>
<td>17.1</td>
</tr>
<tr>
<td>Poland-Warsaw</td>
<td>2.6</td>
<td>3.9</td>
<td>6.9</td>
<td>8.2</td>
<td>15.9</td>
<td>16.8</td>
<td>15.2</td>
<td>18.3</td>
</tr>
<tr>
<td>Denmark-Glostrup</td>
<td>3.7</td>
<td>5.9</td>
<td>6.7</td>
<td>8.2</td>
<td>13.6</td>
<td>15.7</td>
<td>18.8</td>
<td>21.3</td>
</tr>
<tr>
<td>Finland</td>
<td>8.2</td>
<td>12.8</td>
<td>19.5</td>
<td>22.7</td>
<td>28.5</td>
<td>37.3</td>
<td>32.3</td>
<td>32.4</td>
</tr>
<tr>
<td>Northern Sweden</td>
<td>2.9</td>
<td>8.0</td>
<td>10.3</td>
<td>16.2</td>
<td>22.5</td>
<td>28.1</td>
<td>33.1</td>
<td>41.6</td>
</tr>
</tbody>
</table>
**Attack Rates**

For persons aged 25–64 years, the age-adjusted average annual SAH attack rates per 100,000 population for all events are shown in Figure 1 and for men and women separately in Table 2. Taking men and women together, age-adjusted average annual SAH attack rates varied 10-fold among the 11 populations studied, ranging from 2.0 (95% CI 1.6 to 2.4) per 100,000 population per year in the China-Beijing population to 22.5 (95% CI 21.9 to 24.1) per 100,000 population per year in the Finnish population (Figure 1). Age-adjusted average annual SAH attack rates varied 13-fold among men and 10-fold among women in the populations studied. There was no consistent pattern in the sex ratio of attack rates in the different populations (Table 2). Age-adjusted average annual SAH attack rates were essentially the same for men and women in the East Germany, China-Beijing, Yugoslavia-Novis Sad, Italy-Friuli, Sweden-Gothenburg, and Lithuania-Kaunas populations. Age-adjusted average annual SAH attack rates were up to 40% higher in women in the Poland-Warsaw, Northern Sweden, and Denmark-Glostrup populations and up to 80% higher in men in the Finland and Russia-Moscow populations. Age-specific average annual attack rates showed an increase with increasing age in the China-Beijing, Russia-Moscow, Poland-Warsaw, Denmark-Glostrup, Yugoslavia-Novis Sad, and Northern Sweden populations. Age-specific average annual attack rates plateaued in the older age groups (Table 3).

28-Day Case Fatality and Autopsy Rates

Age-adjusted 28-day SAH case fatality rates for the total population of those aged 25–64 years are shown in Figure 2, and for men and women separately in Table 4. There was a 3-fold variation in the age-adjusted 28-day SAH case fatality rates, ranging from 23% (95% CI 13 to 33%) in the China-Beijing population to 62% (95% CI 48 to 76%) in the Yugoslavia-Novis Sad population (Figure 2). For the majority of the populations, there was little difference in the age-adjusted 28-day SAH case fatality rates among men and women (Table 4). However, in the Lithuania-Kaunas and China-Beijing populations, age-adjusted 28-day SAH case fatality was higher in men than women (60% versus 44%, and 28% versus 13%, respectively). A very high case fatality rate was observed during the first days after onset. For the population of the 11 MCCs combined, 1,404 of 3,368 cases of SAH died within 28 days (41.7%). Of these fatal cases of SAH, 37% died within 24 hours, 60% within 48 hours, and 75% within 1 week (Figure 3).

There were 3,070 SAH cases (91.2% of all SAH cases) that survived to receive medical attention. Age-adjusted 28-day SAH case fatality rates for those who survived to receive medical attention are shown in Table 4 (fourth column). There was a 2-fold variation in the age-adjusted 28-day SAH case fatality rates, ranging from 23% (95% CI 13 to 23%) in the China-Beijing population to 51% (95% CI 42 to 60%) in the Russia-Moscow population. For those who survived to receive medical attention, there was little difference between men and women in the age-adjusted 28-day SAH case fatality rates among the individual MCCs except...
for China-Beijing, where the case fatality rate was 2-fold higher in men than in women (data not shown).

Autopsy rates were consistent throughout the period of the study. In the combined population of the 11 MCCs, the autopsy rate was 71% over the period of the study (1982–1995; Table 4). While the autopsy rates were consistent over time in the individual MCCs, there was considerable variability among the MCCs, ranging from 0% in the China-Beijing population to 100% in Lithuania-Kaunas.

Medical Management and Investigation Utilization
For the combined population of the 11 MCCs, 8.8% of SAH cases died before receiving medical attention, 88.7% were managed in hospital, 2.1% were managed at another facility such as a nursing home, and only 0.4% were managed at home (Table 5). The percentage of SAH cases dying before receiving medical attention ranged from 0% in China-Beijing and Denmark-Glostrup to 31.3% in Yugoslavia-Novi Sad. Of the 3,070 cases of SAH who survived to receive medical attention, 2,988 (97.3%) received medical attention in a hospital.

For SAH cases that survived to receive medical attention, Table 6 shows investigation utilization. Taken together, in MCCs with at least 100 cases of SAH, utilization of CT scans increased from 64% (408 cases) in the first 3 years of the study (1983–1985) to 82% (440 cases) in the last 3 years (1992–1994). Over the same periods of time, utilization of lumbar puncture decreased from 65% (415 cases) to 43% (231 cases). Utilization of cerebral angiography varied little during the period of the study; 62% (390 cases) between 1983 to 1985 and 64% (342 cases) between 1992 to 1994.

Discussion
The WHO MONICA Project provides a unique opportunity to perform cross-sectional comparisons of stroke epidemiology in many populations. Although it is truly multinational and the largest study on SAH epidemiology performed so far, it covers only Caucasian populations, with 1 exception (Beijing).

This multinational study of SAH demonstrated significant variation in a number of different epidemiological character-
istics among 11 populations participating in the WHO MONICA Stroke Study. The age-adjusted average annual SAH attack rates (per 100,000 population) in the population of persons aged 25–64 years, varied 10-fold between the China-Beijing and Finland populations. In making this comparison, consideration must be given to the likelihood that the China-Beijing attack rate was an underestimate of the true attack rate. The autopsy rate in China is very low because of cultural tradition, so it is likely that persons with SAH who died before receiving medical attention were not detected. The case fatality rate was also low in the China-Beijing population, particularly among women, which indicates that a substantial proportion of very severe cases of SAH with early death could have been missed. Among the other populations in this study, approximately 10% of SAH cases died before receiving medical attention. Even allowing for an underestimation in the China-Beijing attack rate by 20%, there would still be a close to a 10-fold difference in the attack rates. Information on autopsy rates in cases of sudden death was not systematically collected in all centers. It may be that a small proportion of variations in SAH rates between the populations could be due to some SAH events resulting in sudden death being missed.

As reported in detail in previous publications, the MONICA stroke registers have been extensively validated. For instance, validation of the case-finding procedures have shown that home treatment of stroke is uncommon in the Scandinavian countries, at least in the age ranges covered by the MONICA study. This has been reconfirmed in more detailed local validation studies. In China, Lithuania, and Yugoslavia, a sizeable proportion of all stroke patients are seen by a physician at home before death. MONICA centers that initially entered the stroke component of the project but did not fulfill the quality criteria have been excluded. In the centers remaining in the study, the validations indicate that few strokes occurring outside hospital have been missed. The variations in SAH occurrence reported here are likely to be real rather than a reflection of differences in case ascertainment.

Although there have been at least 53 epidemiologic studies of SAH in other non-MONICA populations, direct comparison of the data in these studies with the attack rates in the individual populations in this study was not appropriate for a number of reasons. Only 36 of these studies were conducted after 1980, which would ensure that there would be widespread availability of CT scanning. Linn et al have shown that high rates of CT scanning are necessary in epidemiological studies of SAH to ensure that case ascertainment is accurate. Of the 36 studies performed after 1980, only 17 included the population of 25- to 64-year-old persons in the population studied, and otherwise met the criteria for adequate epidemiological studies of stroke documented by Malmgren et al. None of these studies was limited only to the population of 25- to 64-year-olds, and none had attack (incident and recurrent cases) or incidence rates age adjusted with Segi’s world population. However, there have been 2 reports on comparisons of SAH incidence between different populations utilizing standardized rates. The use of different standardizing populations means that the data from individual populations in these studies cannot be compared directly, but the variation in rates between the populations within each study could be compared. Ingall and Whisnant used the 1980 United States white population to age-adjust SAH incidence rates in studies in which the entire population was surveyed. They found a 4-fold difference in SAH incidence rates among 8 populations on 3 continents and New Zealand. Using Segi’s European population to age- and sex-adjust SAH incidence rates, Sudlow et al found a 5-fold difference in SAH incidence rates for persons aged 45 to 84 years among 8 populations in 3 continents. Other population-based studies have also shown high SAH incidence rates in Finland compared with other countries.

In general, the age-specific average annual SAH attack rates increased with increasing age, although in the East Germany, Italy-Friuli, Sweden-Göteborg, Lithuania-Kaunas, and Finland populations, the age-specific average annual SAH attack rates plateaued in the older age groups. Unlike stroke overall, where the incidence of stroke has been shown to increase with increasing age in many different populations, the incidence of SAH has had a variable relationship to age in different populations. In SAH epidemiological studies performed after 1980, a plateauing or decrease in SAH incidence rates after age 50 years has been seen in populations in some countries (eg, Japan, Italy, and New Zealand). A continual increase in SAH incidence rates with increasing age has been seen in studies from the United States, Australia, England, Norway, and Sweden. It should be noted that most previous studies on SAH epidemiology were small, with wide confidence intervals around the estimates of age-specific SAH rates, so the differences between age groups could have been by chance only.

The variability in the sex ratio of attack rates observed in this study has also been seen in SAH incidence studies among other populations. In the population of persons aged 25 to 64 years, similar SAH attack rates in men and women have been observed in epidemiological studies performed after 1980 from Australia, Italy, and Japan. In other studies of persons aged 25 to 64 years performed after 1980, women were found to have a higher incidence of SAH in the populations of Auckland and New Zealand and Rochester, Minn (Robert D. Brown, Jr, MD, written communication, 1999).

The reasons behind these variations in SAH attack rates, the relationship between SAH attack rates and increasing age, and the sex ratio of SAH attack rates in persons aged 25 to 64 were not clear. Genetic factors may be responsible for these variations, but more detailed epidemiological studies would need to be performed to further assess this possibility. Because information on the proportion of SAH cases with an aneurysm or arteriovenous malformation was not collected systematically, comparative data on the source of bleeding cannot be given.

It is possible that variations in incidence rates of SAH were related to differences in the prevalence of risk factors among the populations. In a previous study of stroke attack rates and risk factors in persons aged 35 to 64 years in the MONICA Project, considerable variation was found in the proportion of persons with 1 or more cardiovascular risk factors. The risk
factors surveyed included systolic and diastolic blood pressure, cigarette smoking, serum cholesterol levels, and body mass index. That study found that the prevalence of smoking and elevated blood pressure explained a substantial proportion of the variation of stroke attack rates between the MONICA populations. A study of the prevalence of risk factors in the populations in this study and the extent to which any variation in these risk factors contributed to the variation in SAH attack rates is being performed and will be reported separately.

The high early case fatality rate seen in this study has been observed in other studies. For all MCCs combined, 8.8% of SAH cases died before receiving medical attention. For the period 1975–1984, 12% of SAH cases died before receiving medical attention in Rochester, Minn; for the period 1980–1987 in Middle Finland, 13% of SAH cases died before receiving medical attention.

Studies that ascertain only small numbers of SAH cases who die before receiving medical attention are probably underestimating the true occurrence of SAH in the population. Even in cities where every citizen can reach medical facilities within a few minutes, some cases of SAH would be expected to die before receiving medical care. For the 75 000 citizens in Rochester, Minn, emergency medical services can transport patients to 1 of 3 hospitals (including 2 Mayo Clinic Hospitals) in the city within 5 minutes. Even with easy accessibility to state-of-the-art medical facilities with 70 neurologists, 10 neurosurgeons, and numerous CT scanners, 12% of SAH cases in the Rochester population died before receiving medical care in the period 1975–1984. Because medically unattended cases of fatal SAH are diagnosed by autopsy, it is likely that different autopsy practices are the major reason why a population study of SAH would detect low numbers of cases who died before receiving medical attention. With a crude 28-day SAH case fatality rate in the 11 MCCs combined of 41%, it is likely that the 28-day SAH case fatality rate in the China-Beijing was underestimated by up to 25%.

Among the other MONICA populations, the age-adjusted 28-day SAH case fatality rates ranged from 32% in the Sweden-Göteborg population up to 62% in the Yugoslavia-Novisad population. Comparison of case fatality rates from other published studies was not possible, because no other population-based study has published either crude or age-adjusted case fatality rates for persons aged 25 to 64 years. For persons who survived to receive medical attention, there was a 2-fold variation in age-adjusted 28-day SAH case fatality rates. The reasons for this variation in age-adjusted 28-day SAH case fatality rates among those who survived to receive medical care were not known but may reflect differences in medical care. The majority of the MONICA centers had high utilization of CT scans and cerebral angiography, but details of medical care such as the numbers of patients having neurosurgical procedures, the timing of aneurysm clipping, or the numbers of patients receiving calcium channel-blocker therapy were not known.

With use of uniform procedures and methods for ascertaining cases of SAH, this study showed that there was significant variation in age-adjusted SAH attack and 28-day SAH case fatality rates among 25- to 64-year-old persons in 11 MONICA populations. Whether these variations were due to differences in genetics or the prevalence of cardiovascular risk factors among these populations requires further study.

Appendix

Sites and Key Personnel of Contributing MONICA Centers

China. Beijing Heart, Lung, and Blood Vessel Research Institute, Beijing: Wu Zhausu (principal investigator), Wu Yingkai (former principal investigator).

Denmark. Copenhagen County, Center of Preventive Medicine, Glostrup University Hospital: M. Schroll (principal investigator), H. Kirkby, P. Thorsvaldsen.


Germany. Center for Epidemiology and Health Research, Berlin: L. Heinemann (principal investigator), W. Barth (principal investigator), D. Eisenblätter, A. Assmann, E. Classen, H. Schaedlich.

Italy. Institute of Cardiology, Regional Hospital, Udine: D. Vanuzzo (principal investigator), L. Pilotto, G. Cignacco, R. Marinì, G. Zilio.

Lithuania. Kaunas Medical Academy, Institute of Cardiology, Kaunas: J. Bluzhas (principal investigator), D. Rastenyté.

Poland. National Institute of Cardiology, Department of Cardiovascular Epidemiology and Prevention, Warsaw: S.L. Rywick (principal investigator), M. Polakowska, G. Broda, B. Jasinski.

Russian Federation. National Research Center of Preventive Medicine, Moscow: T. Varlamova (principal investigator).

Sweden. Preventive Cardiology Unit, Östra Hospital, Göteborg: L. Wilhelmsen (principal investigator), P. Hamrén, K. Romanus. Department of Medicine, University Hospital, Umeå: K. Asplund (principal investigator), P.O. Wester (former principal investigator), B. Stegmayr, G. Rönnberg.

Yugoslavia. Novi Sad Health Center, Novi Sad: M. Planojevic (principal investigator), D. Javicovici (former principal investigator).


MONICA Data Center. National Health Institute, Helsinki, Finland: K. Kuulasmaa (responsible officer), J. Tuomilehto (former responsible officer), A.-M. Rajakangas, E. Ruokokoski, M. Mähiönen.


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