Are Changes in Mortality From Stroke Caused by Changes in Stroke Event Rates or Case Fatality?
Results From the WHO MONICA Project

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Background and Purpose—Mortality from stroke has been declining over recent decades in most countries, except in Eastern Europe. In this analysis, based on the World Health Organization Monitoring Trends and Determinants in Cardiovascular Disease (WHO MONICA) Project, we explored to what extent these trends are due to changes in stroke event rate and to changes in case fatality.

Methods—The WHO MONICA Project collected standardized data from 14 populations in 9 countries. All acute strokes occurring in men and women 35 to 64 years of age were included. Registration was carried out between 1982 and 1995, resulting in time spans from 7 to 13 years. Trends in event rates and case fatality were calculated as average annual percentage change.

Results—Up to 6-fold differences were observed in stroke mortality. Mortality declined in 8 of 14 populations in men and in 10 of 14 populations in women. An increase in mortality was observed in Eastern Europe. In the populations with a declining trend, about two thirds of the change could be attributed to a decline in case fatality. In populations with increasing mortality, the rise was explained by an increase in case fatality.

Conclusions—In most populations, changes in stroke mortality, whether declining or increasing, were principally attributable to changes in case fatality rather than changes in event rates. Whether this was due to changes in the management of stroke or changes in disease severity cannot be established on the basis of these results. (Stroke. 2003; 34:1833-1841.)

Key Words: fatal outcome ■ mortality ■ stroke ■ trends

Large decreases in mortality from stroke have occurred in most industrialized countries during recent decades.1–3 Although in some cases a decline in stroke incidence seems to explain most of the decline observed in stroke mortality,4,5 in other populations, the incidence did not decrease at all or decreased much less than mortality did.6–9 Thus, changes in stroke mortality seem not to be explained by changes in incidence alone.

Changes in mortality may depend on changes in case fatality, in turn resulting from changes in the natural history in treatment or in the case ascertainment of the disease. The World Health Organization Monitoring Trends and Determinants in Cardiovascular Disease (WHO MONICA Project) was launched at the beginning of the 1980s to “relate the trends in incidence and mortality of stroke to secular trends in populations’ risk factor levels.”10 All suspected stroke events were registered in several populations and classified through the use of a common protocol and strictly standardized methods and criteria. Thus, MONICA data are not so affected by the data quality problems inherent with routine mortality statistics such as changes in coding practices. In this report, MONICA stroke data were used to study whether any changes in mortality from stroke observed during the study period within each population reflected changes in the event rates of stroke or changes in case fatality.

Materials and Methods

The methods of case ascertainment have been published previously.10–13 Briefly, hospitalized cases were identified either from hospital admissions (hot pursuit) or discharge diagnoses (cold pursuit). To identify all nonfatal events, records from outpatient clinics were scrutinized, and general practitioners and other medical services were contacted. All death certificates with a diagnosis of stroke or other diagnoses involving symptoms also caused by stroke were included in the register, and the diagnoses were checked for validity. Quality assurance of the data has been the key element in the WHO

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TABLE 1. Countries, Populations, Registration Years, Average Population Size, Number of Stroke Events, Number of Fatal Events, Proportion of Unclassifiable Fatal Events, and Stroke Quality Score

<table>
<thead>
<tr>
<th>Country*</th>
<th>Population</th>
<th>Abbreviation</th>
<th>Registration Years</th>
<th>Average Population Size, n</th>
<th>All Stroke Events, n</th>
<th>Fatal Stroke Events, n</th>
<th>Unclassifiable Fatal Events, (% of All Fatal Events)</th>
<th>Data Quality Scores</th>
</tr>
</thead>
<tbody>
<tr>
<td>China</td>
<td>Beijing</td>
<td>CHN-BEI</td>
<td>1987–1993</td>
<td>7 289 776</td>
<td>2542 1802</td>
<td>674 526</td>
<td>5</td>
<td>1.30 1.00</td>
</tr>
<tr>
<td>Denmark</td>
<td>Glostrup</td>
<td>DEN-GLO</td>
<td>1982–1991</td>
<td>10 132 912</td>
<td>1168 613</td>
<td>209 136</td>
<td>6</td>
<td>1.30 2.00</td>
</tr>
<tr>
<td>Finland</td>
<td>Kuopio</td>
<td>FIN-KUO</td>
<td>1983–1992</td>
<td>10 95 622</td>
<td>1644 854</td>
<td>290 168</td>
<td>3</td>
<td>1.84 2.00</td>
</tr>
<tr>
<td></td>
<td>North Karelia</td>
<td>FIN-NKA</td>
<td>1982–1991</td>
<td>10 64 167</td>
<td>902 430</td>
<td>218 109</td>
<td>1</td>
<td>1.80 2.00</td>
</tr>
<tr>
<td></td>
<td>Turku/Loimaa</td>
<td>FIN-TUL</td>
<td>1983–1992</td>
<td>10 77 595</td>
<td>889 479</td>
<td>175 120</td>
<td>1</td>
<td>1.88 2.00</td>
</tr>
<tr>
<td>Italy</td>
<td>Friuli</td>
<td>ITA-FRI</td>
<td>1984–1993</td>
<td>10 376 317</td>
<td>2398 1295</td>
<td>743 469</td>
<td>6</td>
<td>1.69 2.00</td>
</tr>
<tr>
<td>Lithuania</td>
<td>Kaunas</td>
<td>LTU-KAU</td>
<td>1986–1995</td>
<td>10 150 306</td>
<td>2142 1428</td>
<td>552 358</td>
<td>11</td>
<td>1.55 0.00</td>
</tr>
<tr>
<td>Poland</td>
<td>Warsaw</td>
<td>POL-WAR</td>
<td>1984–1994</td>
<td>11 201 541</td>
<td>1820 1072</td>
<td>775 516</td>
<td>23</td>
<td>1.03 2.00</td>
</tr>
<tr>
<td>Russia</td>
<td>Moscow</td>
<td>RUS-MOC</td>
<td>1985–1993</td>
<td>9 85 792</td>
<td>855 598</td>
<td>357 241</td>
<td>16</td>
<td>1.05 1.00</td>
</tr>
<tr>
<td></td>
<td>(control)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Moscow</td>
<td>RUS-MOI</td>
<td>1985–1993</td>
<td>9 230 108</td>
<td>2155 1490</td>
<td>935 683</td>
<td>20</td>
<td>1.05 1.00</td>
</tr>
<tr>
<td></td>
<td>Novosibirsk</td>
<td>RUS-NOI</td>
<td>1982–1993</td>
<td>12 53 478</td>
<td>1196 1303</td>
<td>439 376</td>
<td>4</td>
<td>1.25 1.00</td>
</tr>
<tr>
<td>Sweden</td>
<td>Gothenburg</td>
<td>SWE-GOT</td>
<td>1984–1994</td>
<td>11 153 397</td>
<td>1210 621</td>
<td>225 143</td>
<td>9</td>
<td>0.93 2.00</td>
</tr>
<tr>
<td></td>
<td>Northern Sweden</td>
<td>SWE-NSW</td>
<td>1985–1994</td>
<td>10 193 239</td>
<td>2131 1208</td>
<td>319 232</td>
<td>4</td>
<td>1.83 2.00</td>
</tr>
<tr>
<td>Yugoslavia</td>
<td>Novi Sad</td>
<td>YUG-NOS</td>
<td>1983–1995</td>
<td>13 112 618</td>
<td>1603 887</td>
<td>585 402</td>
<td>1</td>
<td>1.75 1.00</td>
</tr>
</tbody>
</table>

*Populations are listed in alphabetical order.

MONICA Project. Quality assessment reports have been produced periodically, and the MONICA Data Centre also checked the consistency of the demographic data and routine mortality statistics submitted by the local population register team. The core data collection included information on the date of onset of the event, duration of symptoms, date of discharge or death, presence of a previous stroke, clinical diagnoses given by the treating physician, diagnostic examinations performed, classification of stroke (definite stroke, no stroke, or unclassifiable event), and classification of the type of stroke given by the register physician.

A total of 14 populations from 9 countries in Europe and Asia collected stroke data in the WHO MONICA Project for periods varying between 7 and 13 years (Table 1). Information was collected in the permanent resident population of the study area in 25- to 64-year age group. Because in many populations there were few or no cases in the 25- to 34-year age group, especially among women, the cases were mostly fatal cases.

One event was specified by the time frame of 28 days from the onset of symptoms. If the patient was still alive on the 28th day, the event was considered nonfatal. All rates and proportions were standardized by methods described later.

Quality Assurance of the Data
Several indicators of data quality were monitored. Altogether, 18 separate items were assessed for the trend quality scores. Among the most important were (1) differences in trends in event rates, case fatality, and mortality, including and excluding unclassifiable data; (2) the ratio of the number of fatal events in the register to the number of stroke deaths in the routine mortality statistics; (3) the proportion of and trends in several coverage items, including the proportion of nonhospitalized events, and the proportion of registered suspected strokes subsequently classified as nonstrokes; (4) the proportion of and trends in diagnostic examinations or necropsy performed to classify the stroke; and (5) the overall quality of the data.

For good coverage of fatal events, we assumed that the ratio between the number of fatal events in the register and stroke deaths in the routine mortality statistics should be at least 1.0. A ratio <0.9 was highly indicative of low coverage of fatal cases, and the registers with such ratios were required to make an extra effort to find the missing fatal strokes. The proportion of unclassifiable fatal events and the final data quality scores, which could vary between 0 and 2.0, for each population are presented in Table 1.

The quality of the demographic data was assessed separately. The primary analyses were done using all events and all populations with equal weighting. The main analyses were then rerun (1) for incident events, ie, first-ever strokes only; (2) excluding subarachnoid hemorrhage (SAH); (3) excluding unclassifiable events from the analyses; (4) excluding first and last years of registration to eliminate any startup or rundown effects; and (5) comparing linear trends between the first and second halves of registration period to test the assumption of linearity separately for each population. Finally, analyses were rerun, excluding the populations with trend score weights or demographic quality scores <1.0.

Definitions
The WHO definition of stroke was used throughout the study. Acute events were classified as definite strokes, unclassifiable events, and no stroke. Stroke subtypes (subarachnoid hemorrhages [SAHs], intracerebral hemorrhages, and ischemic strokes) were considered together. Both definite strokes and unclassifiable events were included in the analyses. Unclassifiable events (Table 1) were “all cases having insufficient supporting evidence of stroke but whom the diagnosis of stroke cannot be entirely excluded.” These were mostly fatal cases.

One event was specified by the time frame of 28 days from the onset of the event. Consequently, recurrent events were defined as new events when the onset was >27 days from the onset of the previous event. A fatal event was defined as death occurring within 28 days from the onset of symptoms. If the patient was still alive on the 28th day, the event was considered nonfatal. All rates and proportions were standardized by methods described later.
Statistical Analysis
Event rates for the 35- to 64-year age group were standardized directly by 5-year groups to the World Standard Population.\(^9\) Confidence intervals (CIs) of the event rates were calculated assuming Poisson distribution for the age-specific rates and using the relation between Poisson and \(\chi^2\) distributions.\(^9\) We calculated trends from the age-standardized annual rates \((r_t)\) using following model\(^21\):
\[
\log r_t = a + bt + e_t
\]
where \(a\), \(b\), and \(e_t\) are the natural logarithm, the coefficient of the trend, and the error term with allowance for extra-Poisson variation.\(^21\,22\) For small changes, \(100b\) represent the estimated annual percentage change in rate.\(^21\)

Case fatality was standardized to the distribution of MONICA events (assigning to the 35- to 44-, 45- to 54-, and 55- to 64-year age groups the following weights: 1/11, 3/11, 7/11). The 95% CIs were calculated from the SE of the weighted sum of binomial variables using the normal approximation. In addition, annual case fatality trends were calculated using log-linear regression, assuming a binomial distribution within age groups, and including an allowance for additional deviation from the regression line, as for trends in event rates.

The mortality rate from stroke (M), stroke event rate (C), and case fatality (F) are related by \(M = C \times F\). With the assumption of constant rates of change, let \(M'\) indicate the average annual absolute change in MONICA mortality rate and thus \(M'/M\) show the relative change (and similarly for \(C'\) and \(F'\)). Then, by calculus,\(^21\)
\[
M'/M = (C'/C) + (F'/F)
\]
The trend in MONICA stroke mortality rate is therefore the sum of the trend in stroke event rates and the trend in case fatality, all expressed as average annual percentage change. In this way, we can distinguish the relative contributions of trends in stroke event rates and case fatality to trends in mortality.

Sensitivity Analysis
The trends for incidence and event rates were similar although somewhat less steep for incidence, indicating that event rates can be used as proxies for incidence rates in assessment of trends. This is especially important in some centers in which the information about previous stroke for fatal events was often missing.

SAH has sometimes been excluded from analyses in stroke studies because it has a different etiology and natural history from the other subtypes of stroke. When we analyzed stroke trends excluding SAH, these results showed no substantial differences compared with the trends based on all subtypes. Excluding “unclassifiable events” also did not affect trends. When we excluded the first and last years of registration, all trends strengthened, especially in women, by 0.5% to 1% per year, which may suggest poorer coverage in the tails of the registration periods. The results for trends obtained in the main analyses may therefore be somewhat conservative.

In tests of the assumption of linearity, the trends in event rates and stroke mortality were not statistically different, although fluctuations were observed. The 1 exception was stroke mortality among North Karelian men (3.2% versus −5.2% per year, \(P = 0.03\)), a result confirmed by routine mortality statistics in that population.

Finally, the correlations between trends calculated after inclusion or exclusion of centers with trend score weights or demographic quality scores below 1.0 were very similar.

Results
During the study period, 22 655 stroke events among men and 14 080 among women were ascertained in the 35- to 64-year age group. Average case fatality over the populations was 28.7% in men and 31.8% in women. The distribution of the stroke cases by population and sex is shown in Table 1.

Stroke Event Rates, Mortality Rates, and Case Fatality
Pooled information on the first 3 and last 3 years of registration is presented in Table 2. At the end of the study period, the stroke event rate was highest in Novosibirsk, Russia, and lowest in Friuli, Italy. There were 3.7- and 6.6-fold differences between the highest and lowest rates in men and women, respectively. Stroke event rates in men were nearly twice those in women in many populations.

Among men, the case fatality of stroke ranged from 12% in northern Sweden to 53% in Moscow Control in Russia. Overall, the case fatality was high in all Eastern European countries. In women, the difference in case fatality of stroke between populations was larger than in men, ranging from 16% in Kuopio to 57% in Moscow Intervention. (Table 2).

At the end of the study period, stroke mortality was highest in Novosibirsk, Russia, followed by the Eastern European populations. The lowest rates were seen in the Swedish, Danish, and Italian populations (Table 2). Mortality from stroke in Novosibirsk was 6.2 times higher in men and 4.6 times higher in women than in Gothenburg, Sweden. Mortality was on average 1.8 times higher in men than in women, ranging from 1.1 times in Northern Sweden up to 2.5 times higher in Moscow Control.

Trends in Event Rates, Case Fatality, and Mortality of Stroke
Table 3 show the trends, separately for each population, in stroke event rates, case fatality, and mortality of stroke, both in the register and in routine mortality statistics. Stroke event rates declined in 9 of 14 populations in men and 8 of 14 populations in women. The decline was statistically significant in only 2 populations among men (Glostrup, Denmark, and Kuopio, Finland) and 3 populations among women (Kuopio, Finland, and the 2 populations in Moscow, Russia). A statistically significant increase in stroke event trends was observed in Gothenburg, Sweden, among men and in Kaunas, Lithuania, among women.

In men, the case fatality of stroke declined in 7 populations, increased in 8, and fluctuated only slightly in 2. Among women, a decline in case fatality was seen in 8 populations, no obvious change was seen in 3, and an increase was observed in 3. The trends in case fatality were statistically significant among men in only 2 populations with declining trends (Friuli, Italy, and Warsaw, Poland) and in 2 with increasing trends (the 2 Moscow populations). Among women, there was a significant downward trend in Friuli, Italy; Warsaw, Poland; and Kuopio, Finland; and a significant increase in the intervention population in Moscow. Within each population, the CIs for the case fatality trends were larger than those for the trends in stroke event rates.

Of the 14 populations, stroke mortality declined in 8 populations among men and 10 populations among women. Stroke mortality increased in all the Eastern European populations except in Warsaw, Poland. An increase in stroke mortality was observed also in Gothenburg, Sweden, among men and in Turku/Loimaa, Finland, among women. In Beijing, China, and in the 9 Western European populations, stroke mortality declined.

Contribution of Trends in Event Rates and Case Fatality to Trends in Mortality
The Figure shows the contributions of changes in event rate and case fatality to mortality after the centers had been ranked.
### TABLE 2. Age-Standardized Average Stroke Attack Rate, Case Fatality, and Mortality Rate

<table>
<thead>
<tr>
<th>Population</th>
<th>Attack Rate per 100 000</th>
<th>Case Fatality, %</th>
<th>Mortality Rate per 100 000</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>First 3 Years</td>
<td>Last 3 Years</td>
<td>First 3 Years</td>
</tr>
<tr>
<td><strong>Men</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FIN-TUL</td>
<td>236 (208–267)</td>
<td>228 (201–257)</td>
<td>23 (18–29)</td>
</tr>
<tr>
<td>RUS-MOC</td>
<td>270 (241–302)</td>
<td>216 (190–245)</td>
<td>32 (26–37)</td>
</tr>
<tr>
<td>RUS-NOI</td>
<td>438 (382–500)</td>
<td>449 (403–500)</td>
<td>27 (21–33)</td>
</tr>
<tr>
<td>SWE-GOT</td>
<td>129 (115–145)</td>
<td>149 (133–165)</td>
<td>17 (13–21)</td>
</tr>
<tr>
<td>SWE-NSW</td>
<td>221 (205–239)</td>
<td>219 (203–236)</td>
<td>16 (12–19)</td>
</tr>
<tr>
<td>YUG-NOS</td>
<td>222 (198–248)</td>
<td>211 (190–233)</td>
<td>37 (31–42)</td>
</tr>
<tr>
<td><strong>Women</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CHN-BEI</td>
<td>175 (163–188)</td>
<td>182 (169–196)</td>
<td>30 (27–34)</td>
</tr>
<tr>
<td>FIN-KUO</td>
<td>189 (167–213)</td>
<td>130 (113–149)</td>
<td>27 (22–32)</td>
</tr>
<tr>
<td>ITA-FRI</td>
<td>63 (63–70)</td>
<td>59 (53–65)</td>
<td>42 (37–47)</td>
</tr>
<tr>
<td>POL-WAR</td>
<td>90 (79–101)</td>
<td>93 (83–104)</td>
<td>54 (48–60)</td>
</tr>
<tr>
<td>RUS-MOI</td>
<td>133 (122–145)</td>
<td>107 (98–118)</td>
<td>39 (35–44)</td>
</tr>
<tr>
<td>SWE-GOT</td>
<td>71 (71–82)</td>
<td>72 (62–84)</td>
<td>24 (17–30)</td>
</tr>
<tr>
<td>YUG-NOS</td>
<td>114 (98–132)</td>
<td>127 (112–144)</td>
<td>48 (40–55)</td>
</tr>
</tbody>
</table>

See Table 1 for explanation of abbreviations. Values in parentheses are 95% CIs.
in terms of trends in mortality from stroke. If stroke mortality was increasing, the increase was almost entirely due to an increase in case fatality. For the countries showing downward trends in mortality, downward trends in stroke event rate also contributed in some populations. The decline in case fatality explained about two thirds of the overall downward trend in stroke mortality in both sexes. The remaining one third of the decline was due to the downward trend in occurrence of stroke.

**Comparison With Routine Mortality Statistics**

Comparisons between the trends in stroke mortality obtained from the MONICA stroke registers and those obtained from routinely collected mortality statistics are shown in Table 3. The trends were similar for both men and women. Nevertheless, there were several populations with diverging trends, suggesting that routine mortality statistics might not be reliable in these countries.

**Discussion**

The main finding of this study was that across all MONICA populations, the decline in case fatality explained two thirds of the decline in mortality. In populations with increasing mortality, this was explained principally by increasing case fatality; however, as discussed below, there were data quality problems in many of the centers with increasing mortality.14 The relatively modest contribution of event rate to the overall trend in mortality was confirmed by the correlation analyses. The study also confirmed the big differences in mortality (in this study, up to 6-fold in men) between countries previously reported from routine mortality statistics.3

Most international comparisons of trends in stroke have relied on routine mortality statistics3-3 or on indirect comparisons of stroke register data that were often collected at different times and with different study designs. In addition, most studies cover only relatively small geographic areas and limited periods. In the WHO MONICA Project, however,
considerable efforts were made to collect comparable population-based data on stroke over a relatively long period of time.

An important feature of population-based registers of stroke is that they can be used to validate routine data, eg, routine mortality statistics or hospital admission and discharge data. In general, there was good comparability between routine mortality statistics and mortality calculated from the MONICA registers, indicating that routine mortality statistics for stroke in these populations are reasonably reliable.

Apart from Beijing and Novosibirsk, all other populations were located in Europe, making the study more European than worldwide. This was due to practical reasons because the WHO supported the coordination of the MONICA Project and centralized data management and quality control, but funds to collect the data had to be found locally.

Are the MONICA stroke results credible? Accurate assessment of trends requires constant quality of a register over the entire study period. The WHO supported the coordination of the MONICA Project and centralized data management and quality control, but funds to collect the data had to be found locally.

Despite all efforts, there are some caveats regarding the present results. Throughout the 10-year MONICA period, stroke diagnosis in the WHO MONICA Project was based on clinical findings (symptoms, signs, and clinical examination) and thus was not dependent on access to more sophisticated diagnostic techniques. This approach made it impossible to follow changes in subtypes of stroke in many populations. The availability of CT scans increased dramatically in most countries during the study period. Increase in the availability and use of CT scans, however, did not relate to trends in event rates (Table 3).

The MONICA stroke data were subjected to thorough quality assessment for use in trend analyses; the data quality scores are shown in Table 1. Overall, the data were judged to have sufficient quality to be used in trend analyses. Also, sensitivity analyses did not show any impact on results when data with lower quality were excluded.

There were big differences in case fatality between the MONICA populations; case fatality was much higher in many Central and Eastern European populations than in the Scandinavian populations. One possible explanation could be a failure to detect (and include) nonhospitalized, nonfatal cases. This would artificially increase case fatality and decrease incidence. For instance, a decrease in event rate associated with an increase in case fatality was seen in the 2 Moscow populations (see the Figure), possibly because of organizational changes in health care. A high proportion of
unclassified fatal cases in Warsaw has probably inflated case fatality and event rates. The center could not validate these out-of-hospital deaths, which were registered from death certificates. On the other hand, previous population-based studies in Central and Eastern European countries have also found high case fatality in acute stroke, with levels similar to those reported in Scandinavia around 1970.26,27 Thus, although the differences in case fatality between MONICA populations may reflect methodological problems, they also reflect true differences across the MONICA populations. A change in the natural history of stroke with less severe manifestations in recent years may have occurred in Western Europe and North America but not in Eastern Europe.

We are aware of the shortcomings of our data set in which only ages up to 65 years were covered. Stroke incidence and mortality increase steeply with age; thus, the MONICA stroke study covers only a minority of strokes. A recent large study assessing international trends in stroke mortality in the 35- to 74- and 75- to 84-year age groups showed similar, although somewhat attenuated, trends in the older compared with the younger age group. Two of the MONICA populations have registered strokes without an upper age limit. In Glostrup, Denmark, the trends in event rates and mortality between subjects 65 to 74 and those ≥75 of age were similar to those of younger age.31 Additionally, in Turku, Finland, stroke incidence and mortality declined up to the age of 84 years, but the number of strokes registered remained stable because of an increase in the average age of the population.32

Increasing mortality and case fatality were seen almost exclusively in the Eastern European countries. Dramatic political and economic changes occurred in these countries during the study period. Such changes have had an impact on the availability of data, making it much more difficult to maintain the same quality during the latter years of registration. However, the MONICA observations on stroke (present results) and coronary heart disease are fully compatible with the decline in life expectancy in post-Soviet bloc countries during the first half of the 1990s, mainly because of increasing mortality rates in cardiovascular diseases.33

The gap between populations with low and high mortality from stroke tended to increase during the study period. The relative contribution to case fatality of changes in management or severity of the disease cannot be derived from our results, but it is likely that both factors are involved. A decline in 28-day case fatality might indicate improved care for acute stroke, especially in-hospital treatment. Stroke units have been shown to improve significantly both the functional outcome and the case fatality after a stroke, but in most countries, they were established after the MONICA data collection period.

Stroke event rates were ~2-fold higher in men compared with women. This ratio is higher than in several other studies. The explanation is that in the present analyses, only data for the 35- to 64-year age group were used; in older age, the ratio diminishes.

In conclusion, our results indicate that changes in case fatality were important for changes in stroke mortality across MONICA populations. This highlights the importance of also obtaining information on nonfatal events when assessing the burden of stroke in a community; mortality does not tell the whole story. The MONICA results emphasize the contribution of prevention and quality of medical care to drive mortality trends. They also raise the possibility that the natural history of stroke is changing, with events becoming less severe in economically advanced countries and more severe in countries experiencing great socioeconomic strain.

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Editorial Comment

Explanations for International Trends in Stroke Mortality

Stroke mortality varies greatly from country to country. In 1985, the highest figures in eastern European countries were 6- to 7-fold those of countries with the lowest mortality rates, and the same trend has continued in the 1990s. The mortality rates have not, however, remained stable during the last decades. In most countries, a significant reduction has occurred, whereas in some countries the opposite is true: during 1970 to 1985, the annual changes ranged from +3.9% to −7.1%, and during 1985 to 1994, from +3.2% to −6.8%. The obvious causes of the reduced mortality rates have been either a decreased incidence of stroke or the case-fatality rate, or both. The explanations for the growing mortality rates, mainly in the eastern European countries, have been more or less speculative.

In the present study, Sarti and associates have answered these questions. Their impressive patient material consisted of 36,000 young (35 to 64 years) acute stroke victims from the WHO MONICA project. The patient data were collected during 1982 to 1995 from 14 centers in 9 countries with as complete case finding as possible. The subtypes of stroke were considered together. The attack rate included all patients, both first-ever and recurrent strokes, and the case-fatality rate was calculated on the basis of patients dying within 28 days of stroke onset.

Age-standardized (World Standard Population) average attack rate (per 100,000 per year), case fatality (%), and MONICA mortality rate (per 100,000 per year) were calculated, as well as the annual trends. MONICA mortality trends were compared with those of official mortality statistics. Both the rates and trends from different centers varied greatly, the highest age-standardized rates being 2- to 6-fold compared with the lowest rates. In two thirds of the centers mortality declined, whereas in one third it remained unchanged or increased.
A comparison of changes in attack and case-fatality rates with changes in mortality rates revealed that two thirds of a decreasing mortality is attributable to reduced case fatality, and one third to reduced attack rate. The increasing mortality rate is almost exclusively explained by an increasing case-fatality rate.

A few points in this excellent study deserve comments. The most important one is the relatively young age structure of the subjects, which represents one third of all stroke cases and only one tenth of all patients dying of stroke. Thus, the results are certainly applicable to young stroke patients, but I am uncertain whether they can be generalized to older age groups.

One of the MONICA centers (Glostrup, Denmark) collected data during 1982 to 1991 on stroke patients of all ages. Both the age-adjusted attack and incidence rates declined significantly in all age groups, and the age-adjusted mortality rates followed the trend of incidence rates. A significantly higher case-fatality rate was, however, observed among recurrent strokes and with increasing age, and the age-adjusted case-fatality rate increased significantly in men and insignificantly in women. On the basis of these results, one can speculate that the inclusion of elderly (>64 years) stroke patients may give the trends of attack and incidence rates a more prominent role in determining mortality trends than in the present study.

Another question is the comparison of MONICA mortality rates with official mortality statistics. The MONICA project is concerned with acute stroke (International Classification of Diseases, 8th and 9th revisions, codes 430 to 434 and 436), and the official statistics include both acute strokes and nonacute cerebrovascular disorders (codes 430 to 438). Furthermore, only deaths within 28 days of stroke onset are counted in the MONICA project. In practice, however, many stroke victims die months or even years after the acute phase of some complication (eg, pneumonia, pulmonary embolism), but stroke appears as the underlying cause on the death certificate. Therefore, it is difficult to comprehend how one MONICA register can obtain, compared with official mortality statistics, a ratio of 1.0 or above in the number of stroke deaths. Obviously, the number of deaths occurring in the study population are extrapolated from the official mortality statistics, but have the nonacute deaths appearing in the official statistics been omitted? An explanation would be needed.

Anyhow, the study by Sarti and colleagues gives important data elucidating the background of stroke mortality trends. Sixty-five percent of the decrease in the mortality rate is explained by a reduced case-fatality rate, and the remaining 35% is attributed to a reduced event rate. Mortality rate increases are almost solely a result of an increased case-fatality rate. The results are valid for young stroke patients. I look forward to a corresponding analysis based on the MONICA centers that have collected data on patients of all ages.

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Editorial Comment—Explanations for International Trends in Stroke Mortality
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