
Ewa Lindenstrøm, MD; Gudrun Boysen, MD, PhD; Jørgen Nyboe, MSc; and Merete Appleyard, RTL

Background and Purpose: Temporal trends in stroke incidence in Denmark have not been previously reported. The Copenhagen City Heart Study is a prospective study based on a randomly selected sample of an urban population of, initially, 19,698 participants followed since 1976. Over a period of 12 years, we studied three important aspects of stroke incidence in 848 identified cases: temporal trends, dependence on age and sex, and comparison of responders and nonresponders.

Methods: The participants were invited to two health examinations at 5-year intervals. The participants who attended at least one of the two examinations are termed responders and those who attended none nonresponders. The cases of first-ever stroke were collected from responders, the National Patient Register, and the National Register of Deaths and were verified by study of hospital records and death certificates.

Results: For responders aged 35–64 years and ≥65 years, there were no significant changes in the weighted rates in four consecutive 3-year periods. There was a tendency toward decreasing rates among younger women, but not in older women or men. The age- and sex-adjusted rates per 1,000 (based on the Danish population in 1982) in responders in the entire 12-year follow-up period were 1.61 in women, 2.67 in men, and 2.14 in both sexes combined. Stroke incidence rates increased exponentially with age in both sexes, with rates in men generally twice those in women, even in the ≥75 years of age group. Age-adjusted rates were higher in nonresponders than in responders. For women, this ratio was 1.7; for men, 1.1.

Conclusions: The stroke incidence in Copenhagen is relatively high and has shown no decreasing tendency over the period 1976–1988. (Stroke 1992;23:28–32)
At the second examination, new cerebrovascular events during the first 5 years of follow-up were identified. The procedure and the complete questionnaire used at the examinations have been described. Additional information on new cerebrovascular events and events prior to the observation period was obtained through the National Health Service Register of Deaths and the National Patient Register. These registers provide unique information on all hospital admissions in Denmark, including patient and hospital unit identification, admission and discharge dates, and six-digit codes corresponding to all discharge diagnoses. However, because the National Patient Register was first established in 1976, information on previous events in nonresponders could be obtained only if they were hospitalized in the observation period and one of the discharge diagnoses referred to previous stroke.

For all the participants diagnosed with codes 430–438 of the World Health Organization’s International Classification of Diseases (8th revision), hospital discharge letters were retrieved to identify those who had suffered an event. When necessary, all hospital records as well as additional information from the patient’s general practitioner, family, or nursing home were collected. After the first 5 years of follow-up, we realized that no strokes could be identified in patients with codes 437 and 438; thus, in the following periods, only codes 430–436 were considered. At the second health examination, 103 stroke survivors were identified. Among these, 25 had not been hospitalized for their first stroke, and the diagnosis was based on history and neurological examination.

Death certificates were obtained from the National Health Service Register of Deaths in all cases in which stroke was registered as either underlying cause or contributing cause of death. Whenever possible, these certificates were supplied by information from other sources as stated above. In 28 cases (seven responders and 21 nonresponders; 3.3%), the diagnosis was verified on the basis of death certificates alone.

For the purpose of this study, we considered all events until December 31, 1988. Only initial stroke was considered for the incidence study, and persons with documented stroke before the initial examination were excluded. Stroke was defined as an acute disturbance of focal or global cerebral function with symptoms lasting >24 hours or leading to death. This definition excludes transient ischemic attack. Consequently, in persons who had both first-ever transient ischemic attack and first-ever stroke in the observation period, only stroke was registered as event. Persons with first transient ischemic attack before the observation period were not excluded.

Subdural, extradural, and traumatic intracranial hematoma, confirmed by cerebral computed tomographic (CT) scan, surgery, or autopsy, were not counted as events; nor was verified primary subarachnoid hemorrhage, although the above definition also refers to this event. Cerebrovascular lesions discovered at autopsy or on CT scan, without previous clinical manifestations of stroke, were not registered as stroke.

The stroke events were identified and classified after critical revision of collected information. Cases too vague to be attributed to stroke were not counted as events. The remaining events were divided into the following categories: hemispheric infarction, hemorrhagic (CT) scan, surgery, or autopsy, were not counted as events; nor was verified primary subarachnoid hemorrhage, although the above definition also refers to this event. Cerebrovascular lesions discovered at autopsy or on CT scan, without previous clinical manifestations of stroke, were not registered as stroke.

Temporal trends in stroke incidence were studied in responders only. For each responder, the follow-up period (1976–1988) was divided into four consecutive 3-year periods. Thus, the beginning of the first period fell chronologically between March 1, 1976, and March 31, 1978. The average annual rates for each sex group and 10-year age group for a given 3-year period were calculated by dividing the number of events in the period by the number of person-years. Events and person-years referred to respondents who were alive and free from stroke at the beginning of the 3-year period.

Person-years for an individual were calculated from the beginning of the 3-year period until stroke, death, or the end of the period. The ages given in the tables are average ages for the 3-year periods. Thus, for example, when the age group 45–54 years is considered in each of the four 3-year periods, it corresponds to the following age groups at the first...
Table 1. Average Annual Sex- and Age-Specific Incidence Rates (per 1,000) of First-Ever Stroke in Four Consecutive 3-Year Follow-up Periods and Entire 12-Year Period

<table>
<thead>
<tr>
<th>Age group (yr)</th>
<th>1</th>
<th>Rate</th>
<th>n</th>
<th>2</th>
<th>Rate</th>
<th>n</th>
<th>3</th>
<th>Rate</th>
<th>n</th>
<th>4</th>
<th>Rate</th>
<th>n</th>
<th>1976–1988</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>35–44</td>
<td>1</td>
<td>0.25</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>1.68</td>
<td>0</td>
<td>0</td>
<td>4</td>
<td>0.41</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>45–54</td>
<td>6</td>
<td>0.91</td>
<td>6</td>
<td>1.07</td>
<td>4</td>
<td>0.80</td>
<td>2</td>
<td>0.49</td>
<td>18</td>
<td>0.85</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>55–64</td>
<td>19</td>
<td>2.34</td>
<td>17</td>
<td>1.97</td>
<td>12</td>
<td>1.57</td>
<td>9</td>
<td>1.48</td>
<td>57</td>
<td>1.87</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>65–74</td>
<td>17</td>
<td>4.52</td>
<td>33</td>
<td>7.22</td>
<td>31</td>
<td>5.49</td>
<td>29</td>
<td>4.69</td>
<td>110</td>
<td>5.45</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>75–84</td>
<td>5</td>
<td>9.65</td>
<td>5</td>
<td>5.87</td>
<td>18</td>
<td>9.70</td>
<td>32</td>
<td>13.89</td>
<td>60</td>
<td>10.85</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>35–44</td>
<td>2</td>
<td>0.55</td>
<td>3</td>
<td>1.12</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0.93</td>
<td>6</td>
<td>0.66</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>45–54</td>
<td>11</td>
<td>2.06</td>
<td>7</td>
<td>1.48</td>
<td>10</td>
<td>2.29</td>
<td>4</td>
<td>1.11</td>
<td>32</td>
<td>1.78</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>55–64</td>
<td>30</td>
<td>4.78</td>
<td>29</td>
<td>4.75</td>
<td>34</td>
<td>6.25</td>
<td>22</td>
<td>5.03</td>
<td>115</td>
<td>5.18</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>65–74</td>
<td>36</td>
<td>10.39</td>
<td>46</td>
<td>11.62</td>
<td>36</td>
<td>8.63</td>
<td>41</td>
<td>9.88</td>
<td>159</td>
<td>10.10</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>75–84</td>
<td>9</td>
<td>19.31</td>
<td>18</td>
<td>28.08</td>
<td>32</td>
<td>25.62</td>
<td>20</td>
<td>13.13</td>
<td>79</td>
<td>20.37</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Data are from responders in the Copenhagen City Heart Study, 1976–1988. n, Number of strokes.

Discussion

Our study fulfills most of the "ideal" criteria set up by Malmgren et al.6 Because the primary health
stroke incidence rates were higher, whereas rates were lower in the other "ideal" studies.\textsuperscript{8-13} The high rates in our study can be explained only partially by the high proportion of older people in the Danish population.

Age-specific incidence rates of first-ever stroke were also highest in Shibata,\textsuperscript{7} closely followed by Söderhamn (1983–1984)\textsuperscript{8} and the present study. Rates in Rochester, Minnesota; Tilburg, The Netherlands; Espoo–Kauniainen, Finland; Auckland, New Zealand; Oxfordshire, England; Benghazi, Libya; and Umbria, Italy,\textsuperscript{15} were lower.

When both age- and sex-specific rates are considered, the rates in our study were approximately two times higher in men than in women, even in the higher age groups.

Recent stroke studies from other parts of Scandinavia similarly show a twofold higher incidence in men than in women (K. Asplund, personal communication). In most earlier studies, however, the ratio between incidence rates in men and women decreases with age. Thus, for the age group 75–84 years, the male-to-female ratio in our study was 1.9 in comparison with ratios between 1 and 1.3 in other studies.\textsuperscript{8,10-13,15} Among the 103 stroke survivors identified at the second examination, the proportion of nonhospitalized cases was 38% (15 of 40) in women and 16% (10 of 63) in men. This could indicate that women with stroke in the study population were less likely to be hospitalized than men. However, it is not possible to draw definite conclusions because the 103 cases represent only 12% of the 848 strokes identified. We are at present analyzing the risk factors for stroke in the study population and will soon be able to report whether they differ from those found in other countries.

In the present study, stroke incidence showed no significant changes in time, although a tendency for decline was seen in younger women. To our knowledge, no other changes could account for the temporal trends; neither the number of medical facilities nor available physicians has increased in Copenhagen during the study period. Modern technology cannot account for the missing decline either, as the diagnosis of stroke was based on clinical criteria. Magnetic resonance imaging was not used as a diagnostic tool for stroke. The use of CT scanning increased in the last years, but in our study it served mainly to distinguish between stroke subtypes. In no case was stroke identified on the basis of CT results alone if not preceded by relevant clinical signs. The results from Rochester showed that the decline in stroke incidence between 1945 and 1979 has stopped, and an increasing trend occurred in 1980–1984.\textsuperscript{9} In Japan, a decline of stroke incidence has been reported from two regions: Hishayama,\textsuperscript{16} between 1961 and 1976, and Ikawa,\textsuperscript{17} between 1965 and 1983. In contrast, in Söderhamn,\textsuperscript{8,18} there was a significant increase in incidence rates for women but no change for men or for the total population between 1975 and 1978 and between 1983 and 1986.
The design of the Copenhagen City Heart Study made possible the comparison of stroke incidence in responders and nonresponders. Responders constituted 79% of the study population. The ratio of stroke incidence rates, adjusted to the study population, between nonresponders and responders was 1.7 in women but only 1.1 in men. One explanation might be that stroke is a stronger selective factor in women than in men, preventing more women than men from attending the health examinations. Stroke severity and social factors, combined with the illness, might be the reason. Another explanation is that health examinations may have a stronger intervention effect in women than in men by influencing health awareness and contacts with the health sector and, thus, reducing risk factors. Part of the higher incidence rates in nonresponders might also be attributed to failure of excluding cases with nonrecognized previous stroke.

The differences between responders and nonresponders in the study population have been discussed previously. Nonresponders had a higher mortality in all age groups and in both sexes. It seems, therefore, that the higher stroke incidence in nonresponders is real.

Acknowledgments

We are indebted to Gorm Jensen, MD, PhD, and Peter Schnohr, MD, who initiated and conducted the Copenhagen City Heart Study.

References


Key Words • cerebrovascular disorders • epidemiology
E Lindenstrøm, G Boysen, J Nyboe and M Appleyard

Stroke. 1992;23:28-32
doi: 10.1161/01.STR.23.1.28

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/23/1/28