Incidence, risk, and case fatality of first ever stroke in the elderly population. The Rotterdam Study

M Hollander, P J Koudstaal, M L Bots, D E Grobbee, A Hofman, M M B Breteler

Methods: The authors conducted a study in 7721 participants from the population based Rotterdam Study who were free from stroke at baseline (1990–1993) and were followed up for stroke until 1 January 1999. Age and sex specific incidence, case fatality rates, and lifetime risks of stroke were calculated.

Results: Mean follow up was 6.0 years and 432 strokes occurred. The incidence rate of stroke per 1000 person years increased with age and ranged from 1.7 (95% CI 0.4 to 6.6) in men aged 55 to 59 years to 69.8 (95% CI 22.5 to 216.6) in men aged 95 years or over. Corresponding figures for women were 1.2 (95% CI 0.3 to 4.7) and 33.1 (95% CI 17.8 to 61.6). Men and women had similar absolute lifetime risks of stroke (21% for those aged 55 years). The survival after stroke did not differ according to sex.

Conclusions: Stroke incidence increases with age, also in the very old. Although the incidence rate is higher in men than in women over the entire age range, the lifetime risks were similar for both sexes.
complete improvement within 72 hours or documented atrial fibrillation at time of the stroke.

**Data analysis**

The age specific incidence rate was obtained for each five year band by dividing the number of strokes by the total amount of person years attributed to a specific age category. The follow up ended either at occurrence of stroke, or at death, or at 1 January 1999, whichever came first. Participants who suffered from a subarachnoidal haemorrhage were censored on the date of the event. Incidence rates are given with 95% confidence intervals (CI), assuming Poisson distribution. We calculated incidence and 28 days case fatality rates for subtypes of stroke in 10 year age ranges. For the calculation of 52 weeks case fatality rates we restricted ourselves to cases that occurred before 31 December 1998. We used Cox proportional hazards regression to investigate sex differences in risk of stroke and survival after stroke. In these analyses we adjusted for age at baseline and stroke, respectively. Survival after stroke was calculated using the Kaplan-Meier method. To calculate the absolute risk of stroke over time we took the competing risk of dying into account. Firstly, we obtained the stroke free survival at different ages from the cohort with the Kaplan-Meier method. Age at baseline was used as entry time and age at end of follow up, occurrence of stroke, or death as failure time. Then the cumulative absolute risk of stroke over a period was calculated as the integrated product of the age specific stroke incidences and the stroke free survival. The risk of stroke over time was calculated separately for men and women at ages 55, 65, 75, and 85 years.

**RESULTS**

The mean follow up time was 6.0 years. We had 46 011 person years of observation and 432 suffered from a first ever stroke. Of these 39 were primary intracerebral haemorrhages (9.0%), 233 cerebral infarctions (53.9%), and 160 unspecified strokes (37.0%). A CT or MRI scan was performed in 256 (59.3%) cases and in two cases necropsy was performed. The haemorrhages and infarctions were confirmed by neuroimaging in 74.4% and respectively 94.4%. A total of 256 persons (59.3%) were hospitalised. The incidence rate of stroke increased with age and ranged from 1.7 (95% CI 0.4 to 6.6) in men aged 55–59 years to 69.8 (95% CI 22.5 to 216.6) in men aged 95 or over (table 1). Corresponding rates for women were 1.2 (95% CI 0.3 to 4.7) and 33.1 (95% CI 17.8 to 61.6), respectively. Incidence rates were higher in men than in women over the entire age range. Adjusted for age at baseline the relative risks of stroke for men compared with women in partipants aged younger and older than 75 years were respectively 1.64 (95% CI 1.26 to 2.15) and 1.36 (95% CI 1.02 to 1.83). Table 2 shows that the incidence rate increased with age until the age of 85 for all subtypes of stroke. After age 85, the proportion of unspecified strokes became very high and estimates of the frequency of subtypes of stroke less reliable. The proportion of hospitalised strokes decreased with age in both sexes (fig 1).

**Case fatality**

The overall 28 days case fatality rate was 32.5% for all strokes, 12.4% for cerebral infarctions, and 33.3% for cerebral haemorrhages. Corresponding 52 week case fatality rates were 40.4, 23.6, and 62.9%. We observed no difference in survival after stroke between men and women (fig 2). Case fatality rates of stroke, cerebral infarction, and intracerebral haemorrhage increased with age (table 3).

** Lifetime risk of stroke**

Figure 3 shows survival and stroke free survival for 55 and 75 years old participants as observed in the total study cohort. The areas between the survival and stroke free survival curves represent the average time subjects live after a stroke. The area
comprised 3.45 (95% CI 2.93 to 3.97) years for men and 3.12 (95% CI 2.69 to 3.55) years for women aged 55 years. Corresponding figures for persons aged 75 years were 2.16 (95% CI 1.59 to 2.73) and 2.10 (95% CI 1.63 to 2.57) years, respectively. Table 4 shows the cumulative incidence of stroke over time for men and women at different ages. The absolute risk of getting a stroke is nearly similar for men and women in all age categories, reflecting higher incidence rates, but shorter life expectancy in men as compared with women.

DISCUSSION
We found that the incidence rate of stroke was higher in men than in women over the entire age range. Nevertheless, as a net result of a shorter life expectancy and a higher incidence rate of stroke in men as compared with women, lifetime risks of stroke in men and women were similar at different ages.

Case ascertainment
Studies on incidence of stroke are vulnerable to selection bias. Although our participation rate was high (78%), it is conceivable that non-participants had a higher risk profile for stroke. Consequently, our incidence figures most probably are conservative estimates of the true population incidence of stroke. Complete and accurate case ascertainment is crucial for the validity of the results of an incidence study. The prospective study design, standard definitions, defined study population, and multiple methods of case finding were in accordance with core criteria proposed by Malmgren and colleagues.14 Furthermore, the investigation and characteristics of stroke in this study fulfil criteria for optimal case ascertainment defined by researchers from the WHO MONICA stroke study.15 The follow up was complete for all participants and we used extensive and overlapping case finding methods to reduce selection bias in follow up. The proportion of non-hospitalised strokes in our study was 39%. This is in accordance with the proportion (46%) found by the Oxfordshire Stroke Project.16 Rotterdam with nearly 700 000 inhabitants did not have a specific stroke admission strategy during the study period. The low admission rate was mainly explained by a shortage of hospital beds and by the fact that stroke units and stroke services were not yet widespread available and thrombolytic therapy not yet an established treatment. A weakness of our study that results from the fact that not all strokes were hospitalised is the comparatively low proportion of CT or MRI confirmed strokes. We observed that the proportion of unspecified strokes increased with age. Restriction to only neuroimaging confirmed strokes would have led to an underestimation of the incidence, especially in the very old. As only 75% of the intracerebral haemorrhages

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Incidence rate of subtypes of stroke</th>
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<tbody>
<tr>
<td>Age</td>
<td>Cerebral infarction</td>
</tr>
<tr>
<td></td>
<td>Number of cases</td>
</tr>
<tr>
<td>55–64</td>
<td>17</td>
</tr>
<tr>
<td>65–74</td>
<td>72</td>
</tr>
<tr>
<td>75–84</td>
<td>111</td>
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<tr>
<td>85+</td>
<td>33</td>
</tr>
<tr>
<td>All</td>
<td>233</td>
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</table>

*Rate per 1000 person years. †CI, confidence intervals.

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Twenty eight day case fatality for stroke, subtypes of stroke, and hospitalised strokes</th>
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</thead>
<tbody>
<tr>
<td>Age</td>
<td>Stroke</td>
</tr>
<tr>
<td></td>
<td>Number/total</td>
</tr>
<tr>
<td>55–64</td>
<td>2/22</td>
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<tr>
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<tr>
<td>85+</td>
<td>35/117</td>
</tr>
<tr>
<td>All</td>
<td>111/342</td>
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</tbody>
</table>

Figure 1  Incidence rate per 1000 person years for stroke and hospitalised stroke in relation to age in men and in women.

Figure 2  Cumulative survival after stroke according to sex, adjusted for age at stroke.
were confirmed by CT or MRI, the overall results on haemorrhages should be regarded carefully. Almost 95% of the cerebral infarctions were CT confirmed. Therefore, we feel that the overall figures on cerebral infarctions are reliable. However, incidence figures of stroke subtypes in the very old are less reliable.

**Stroke incidence studies**

One hospital based study in the Netherlands (1978–1980) reported comparable, though slightly higher incidence rates of stroke than our study, but did not analyse the very old.\(^2\) Possibly the incidence has declined during the time interval between both studies. The incidence rates found in our study are in accordance with the results from other studies in Europe, although some studies reported lower incidence rates in subjects >85 years.\(^2\)–\(^18\) Studies in Eastern Europe reported higher incidence rates in subjects younger than 85 years, and lower rates in subjects older than 85.\(^2\)–\(^6\) Incidence rates in Eastern European countries are known to be higher than in Western Europe. The lower rates in the very old in other studies might be explained by under-report of stroke in the elderly population, as we have shown that the proportion of hospitalised strokes declines with age. Incidence rates of stroke in subjects with a European background in Auckland, New Zealand (1992) were higher than in the Rotterdam Study.\(^2\) However, the North East Melbourne Stroke Incidence Study (1996–1997) reported similar rates.\(^3\) In our study the survival after stroke was equal in men and women. Most other studies did not find sex differences either.\(^2\)–\(^4\) We observed an increasing case fatality with age, and a higher case fatality of cerebral haemorrhages as compared with cerebral infarctions. These results are in accordance with results from other studies.\(^2\)–\(^6\)–\(^1\)–\(^8\)

**Lifetime risk of stroke**

Our calculations of lifetime risks of stroke were based on the assumption that characteristics of the cohort remain constant over time. They showed that although the incidence rate of stroke in men was higher than in women, the lifetime risk to get a stroke was similar when we took the competing risk of dying into account. The higher incidence rate of stroke is counterbalanced by shorter survival in men as compared with women. As a consequence, women on average are older when they get a stroke. In conclusion, stroke incidence increases with age, also in the very old. Although incidence rates in men were higher than in women over the entire age range, lifetime risks were similar.

**ACKNOWLEDGEMENTS**

This study has been supported by the Research Institute for Diseases in the Elderly, funded by the Ministry of Education and Science and the Ministry of Health, Welfare and Sports, through the Netherlands Organisation for Scientific Research (NWO). Dr M Hollander is supported by grant 904–61–091 of the NWO. Dr M L Bots is in part supported by grant 96.141 of the Netherlands Heart Foundation. Dr M M B Breteler is a fellow of the Royal Netherlands Academy of Arts and Sciences.

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Competing interests: none declared.

**REFERENCES**


**Table 4** Period and lifetime risk of stroke for 55, 65, 75, and 85 year old men and women taking competing risk of death into account

<table>
<thead>
<tr>
<th>Age</th>
<th>Period risk (%)</th>
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<td></td>
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<tr>
<td>Men</td>
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<td>75</td>
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</tr>
<tr>
<td>85</td>
<td>6.8</td>
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</tbody>
</table>
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*J Neurol Neurosurg Psychiatry* 2003 74: 317-321
doi: 10.1136/jnnp.74.3.317

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